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CONTENTS FOR APRIL, 1934

Original Communications

Syphilitic Disease of the Coronary Arteries. Howard G. Bruenn, M.D., New York, N. Y. ---- 421

Study of Glucose Therapy in Heart Failure in Advanced Cardiac Disease. Abigail Eliot Smith, M.D., and Drew Luten, M.D., St. Louis, Mo. ---- 437

Electrocardiograms That Represent the Potential Variations of a Single Electrode. Frank N. Wilson, M.D., Franklin D. Johnston, M.D., A. Garrard Macleod, M.D., and Paul S. Barker, M.D., Ann Arbor, Mich. ---- 447

The Significance of Electrocardiograms Characterized by an Abnormally Long QRS Interval and by Broad S-Deflections in Lead I. Frank N. Wilson, M.D., Franklin D. Johnston, M.D., Ian G. W. Hill, M.B., A. Garrard Macleod, M.D., and Paul S. Barker, M.D., Ann Arbor, Mich. ---- 459

Electrocardiograms of an Unusual Type in Right Bundle-Branch Block. Frank N. Wilson, M.D., Franklin D. Johnston, M.D., and Paul S. Barker, M.D., Ann Arbor, Mich. ---- 472

Primary Sarcoma of the Heart. Arlie R. Barnes, M.D., Donald C. Beaver, M.D., and Albert M. Snell, M.D., Rochester, Minn. ---- 483

Rupture of Normal Chordae Tendineae of the Mitral Valve. Channing Frothingham, M.D., and George M. Hass, M.D., Boston, Mass. ---- 492

Observations on the Duration of the Phases of Diastole in Man. Anne Bohning, M.D., and Julian Plaut, M.D., Chicago, Ill. ---- 500

The Precordial Lead in 104 Normal Adults. Arthur M. Master, M.D., New York, N. Y. ---- 511

The Effect of Condensers in the Electrocardiograph. Myron Schwarzschild, M.A., and Milton Kissin, M.D., New York, N. Y. ---- 517

A Self-Retaining Skin Contact Electrode for Chest Leads in Electrocardiography. Irving R. Roth, M.D., New York, N. Y. ---- 526

An Efficient Apparatus for Simultaneous Electrocardiographic and Arterial Pulse Records. J. Edwin Wood, Jr., M.D., and R. J. Gentile, B.S., University, Va. ---- 530

Department of Clinical Reports

Coarctation of the Aorta. Harold L. Stewart, M.D., and S. Bellet, M.D., Philadelphia, Pa. ---- 533

Sclerosis of the Coronary Arteries With Myocardial Infarction in a Young Woman. H. W. Rathe, M.D., Waverly, Iowa ---- 539

Correspondence

A Plea for Uniformity in the Biological Standardization of Commercial Preparations of Digitalis ---- 542

Department of Reviews and Abstracts

Selected Abstracts ---- 544

Book Reviews ---- 556

The American Heart Journal

VOL. 9 APRIL, 1934 NO. 4

Original Communications

SYPHILITIC DISEASE OF THE CORONARY ARTERIES*†

HOWARD G. BRUENN, M.D.
NEW YORK, N. Y.

INTRODUCTION

AN ABUNDANT literature has appeared in recent years dealing with various aspects of cardiovascular syphilis. Relatively little, however, has been recorded concerning syphilitic disease of the coronary arteries, and a satisfactory correlation between the clinical and pathological features has not been established. It is the purpose of this paper to define the rôle of this affection in relation to the general picture of syphilis of the heart and aorta.

Anatomically, syphilitic disease of the coronary arteries manifests itself in two ways: (1) obstruction to the coronary blood flow by stenosis or occlusion of the orifices of the coronary arteries, and (2) syphilitic involvement of the branches distal to the orifices. The rôle of syphilis in producing lesions of the latter type is of questionable importance. Warthin,[1] who maintained that localized syphilis of the smallest arterioles is an essential part of the general pathological condition of chronic or latent syphilis, added that "syphilis of the coronary arteries, in our experience, has been found much less frequently than anticipated from its frequent mention in the literature. . . . the larger branches of the coronaries only rarely show lesions that can be recognized as syphilitic." Maher[2] described changes of the larger branches of the coronary arteries similar to those found in the aorta. Moritz[3] recently reported cases with like findings in those portions of the coronary arteries just outside the aorta. On the other hand, Martland,[4] Clawson and Bell,[5] Leary and Wearn,[6] and Coombs[7] concluded that syphilitic coronary disease, except for involvement of the orifices, was rare. Scott[8] stated that "it is interest-

*Submitted in partial fulfillment of the requirements for the degree of Master of Science in the Faculty of Medicine, Columbia University.

†From the Department of Medicine, College of Physicians and Surgeons of Columbia University, and the Presbyterian Hospital.

ing to note that in spite of the active disease surrounding their orifices, the coronary vessels themselves were seldom involved.''

The study of our material has indicated that syphilis of the coronary arteries distal to their orifices is an uncommon lesion and is rarely of clinical importance. This paper will, therefore, concern itself only with syphilitic stenosis or occlusion of the coronary orifices.

While the involvement of the aorta by syphilis was first suspected by Paré[9] and Morgagni,[10] the significance of this process in occluding the coronary arteries at their orifices has only recently been stressed. The first observations appeared about the latter part of the nineteenth century and were in the form of pathological reports, such as those quoted by Allbutt[11] and O'Sullivan.[12] Further interest in this type of coronary involvement was stimulated by the two cases reported by Cannon[13] in 1929, and more particularly, by the paper of Leary and Wearn[6] published in the same year.

MATERIAL*

The material on which this study is based includes all of the cases of syphilitic cardiovascular disease which came to autopsy in the Presbyterian Hospital between the years 1910 and 1932, inclusive. During this period, 3,190 autopsies were performed of which 148 showed syphilitic involvement of the heart and aorta, an incidence of 4.6 per cent. The figure approximates those reported by other writers.

TABLE I

INCIDENCE OF CARDIOVASCULAR SYPHILIS AT AUTOPSY

AUTHOR	LOCALITY	NO. OF AUTOPSIES	NO. OF CASES WITH CARDIOVASCULAR SYPHILIS	PER CENT
Symmers[15]	New York	4,880	175	3.5
Reid[16]	Boston	1,678	54	3.2
Cowan and Faulds[17]	Glasgow	1,000	60	6.0
Cullinan[18]	London	1,000	33	3.3

The degree of narrowing of the coronary orifices was variable. There were only 8 cases in the entire group of 148 which showed extreme stenosis or complete occlusion of the right or the left coronary openings. There was a considerable number, however, with a sufficient degree of stenosis to have produced serious embarrassment to the coronary blood flow during life. Clawson and Bell[5] in a similar group of cases published in 1927 give approximate values for the extent of the narrowing expressed in terms of fractions of the normal, but make no mention of a method of measurement. Moritz[3] and Saphir and Scott,[19] in their series of cases, describe the extent of the narrowing merely as ''some stenosis'' of the coronary orifices.

*Part of this material has already been studied from another viewpoint by Lamb, Turner, Golden and Von Glahn.[14] The discrepancies between their figures and the following are accounted for by the longer time period covered in the present series of observations.

The size of a normal coronary orifice has not been clearly defined. In the absence of a normal standard for comparison it is impossible to recognize the lesser degrees of narrowing or to estimate the degree of stenosis. By means of a small, cone-shaped piece of steel, the circumference of which was calibrated in millimeters, it was possible to measure with a fair degree of accuracy the orifices of the coronary arteries in terms of their circumferences. From the inner surface of the aorta, this instrument was inserted as far as possible into the mouths of the coronary arteries. Care was taken that the tip should not be obstructed within the vessel itself, and just enough pressure was exerted to have the instrument fit snugly into the opening. The measurement of the orifice was read from the calibrations on the instrument. Fortunately, 118 hearts of the 148 cases of cardiovascular syphilis had been preserved, and these specimens were measured as described.

In addition, 25 nonsyphilitic cases of similar age groups were selected as a control series, these cases presenting varying pictures of disease, different weights of hearts, with and without arteriosclerosis of the aorta, but with no obstruction to the mouths of the coronary arteries. In measuring this control group, it was found that the average coronary artery orifice measured about 10 mm. in circumference. The normal range was from 8 to 11 mm.

TABLE II

MEASUREMENTS OF CORONARY ORIFICES IN 118 CASES OF AORTIC SYPHILIS

	NO. CASES WITH NORMAL ORIFICES	PER CENT	NO. CASES WITH MARKED STENOSIS	PER CENT
Simple aortitis	40	50.6	4	10.3
Aortitis with aortic valve involvement	18	22.8	25	64.1
Aortitis with aortic valve involvement with aneurysm	10	12.6	9	23.0
Aortitis with aneurysm	11	14.0	1	2.6
Totals	79	100	39	100

Carr,[20] in a group of 119 cases of cardiovascular syphilis, found coronary orifice involvement in 10 (8.4 per cent). Clawson and Bell[5] reported 25 cases of sudden death from closure of the coronaries in a series of 126 cases, an incidence of 19.8 per cent. In Martland's[4] group of 101 cases, the coronaries were involved in 15 (14.9 per cent). In the series studied by Saphir and Scott,[15] 37 out of 107 cases of luetic aortitis (35 per cent) were found to have narrowed coronary orifices.

In the present series of 118 hearts, 42 (35.6 per cent) showed patent coronary orifices measuring over 10 mm. in circumference; in 37 cases (31.4 per cent) one or both openings ranged between 8 and 10 mm.;

while 39 cases (33.0 per cent) had coronary orifices one or both of which measured 7 mm. or less in circumference. This gives a total normal group of 79 cases (66.9 per cent) and 39 cases (33.1 per cent) with stenosed orifices.

This table shows a significant yet obviously logical fact. Syphilis involving the aortic valve is often accompanied by narrowing of the coronary orifices. Of the 39 cases showing definite stenosis to complete occlusion, 34, or 87.1 per cent, also showed involvement of the aortic valves by the luetic process. This frequent association of aortic insufficiency with coronary orifice involvement has been commented upon by most authors. Furthermore, of the 5 cases showing stenosis of the coronary orifices but with no aortic regurgitation, 4 patients never complained of any cardiac symptoms and died of various affections, quite unrelated to heart disease (cirrhosis of the liver, carcinoma, brain tumor and paralytic ileus). Thus, a consideration of syphilitic coronary orifice involvement resolves itself into a discussion of aortic insufficiency with and without this complication.

PATHOLOGY

In most of the forms of obliterative endarteritis of vessels of the size of the coronaries, occlusion depends upon the formation of a thrombus which subsequently undergoes organization. For example, accompanying and following senile involution of the uterus and ovaries, an active endarteritis usually occurs but thrombosis is often a factor in leading to occlusion of the vessel. In thromboangiitis obliterans, as well as in syphilitic disease of the cerebral vessels, thrombosis is the usual process by which the lumen of the vessel is closed. On the other hand, closure of the coronary arteries due to syphilis is always caused by encroachment on the orifices of the arteries by supravalvular sclerosis of luetic origin.

Microscopically, the process is similar to that seen in other portions of the aorta. There occurs an obliterative endarteritis of those vasa vasorum which penetrate the muscular coat of the coronary arteries. The consequent impairment of blood supply leads to nutritional disturbances which are localized to those portions of the coronary vessels which lie within the aortic wall. A progressive increase of the subendothelial layer of the coronary intima takes place which narrows the lumen of the vessel until total occlusion may result. The process preserves intact the endothelial lining of the coronary lumen, so that thrombosis does not occur.

In these cases, interference with efficiency of the coronary blood flow becomes marked. The process of occlusion is very gradual, however, and a collateral circulation may be set up, in part, perhaps, through the Thebesian vessels.[21] The fact that the closure progresses slowly explains the comparative immunity of the patient from symp-

toms and the remarkable freedom of the myocardium from scarring, although the coronary circulation is impaired.

In a series of 20 cases, Clawson and Bell[5] noted 4 in which there was complete closure of coronary orifices—4 of the right, none of the left. Reid[22] reported 5 similar cases—3 of the right, one of the left, both in one. Cannon's[12] two cases showed occlusion of the left in one case, of the right in the other. In the two cases reported by Leary and Wearn[6] the right coronary orifice was occluded in both, the left in one. Of the 39 cases of this series in which stenosis of the coronary orifices was present (the circumference being 7 mm. or less) the right coronary artery was involved in 9 cases, the left in 4, and both orifices were affected in 26 cases. If only total occlusion is considered, the right coronary orifice was obliterated in 8 cases, the left in one. A compilation of these statistics, including the present series, leaves the right occluded in 19 cases, the left in 5. There is no apparent explanation at the present time for the greater frequency and severity of right coronary orifice involvement.

As the syphilitic process usually stops at the upper level of the sinus of Valsalva except for penetration along the attachments of the valves, an abnormally high origin of the coronary arteries might well be an important factor in the involvement of their orifices. That this inference is borne out by the facts was first pointed out by Von Glahn[23] in 1923, and is shown in Table III.

TABLE III

POSITION OF THE CORONARY ORIFICES IN RELATION TO THE UPPER LEVEL OF THE SINUS OF VALSALVA*

	ABOVE		AT		BELOW	
	L.	R.	L.	R.	L.	R.
Coronary orifices patent (42 cases) over 1 cm.	3	6	6	4	14	12
Slight stenosis (37 cases) 8-10 mm.	15	10	3	2	13	17
Marked stenosis (39 cases) 7 mm. or less	17	13	3	4	3	4

*These cases include in part those reported by Von Glahn[23] in 1923, as well as those in his later publication.[14]

The most conspicuous anatomical change noted in the myocardium with aortic insufficiency is cardiac hypertrophy, especially of the left ventricle. The average increase in weight of the heart is fully as great as that found in cardiac failure associated with hypertension. This hypertrophy appears to be the result of aortic regurgitation. The smallest and largest heart in the group with stenosed orifices and in that with normal orifices weighed about the same, respectively 250 and 1,100 gm., yet as seen in Table IV, on the average the hearts with stenosed coronary orifices were less heavy.

TABLE IV

STATE OF THE MYOCARDIUM IN 62 CASES OF SYPHILITIC AORTIC INSUFFICIENCY

	NORMAL CORONARY ORIFICES (28 CASES)	STENOSED CORONARY ORIFICES (34 CASES)
Aortic ring	7.72 cm.	7.75 cm.
Weight of heart	711 gm.	577 gm.
Gross myocardial fibrosis		
none	20	21
slight	4	4
moderate	2	1
marked	1	1
infarction	1	2

It is conceivable that interference with the blood flow through the coronary arteries diminishes the ability of the heart to enlarge. Arteriosclerosis of the coronary arteries was approximately of the same frequency in both groups. Aschoff bodies in the myocardium were found in 3 cases of the group with normal orifices, in one case with stenosed coronary orifices. Hypertension was no more frequent in one group than in the other. It will be shown that no great variation exists in the average of the two groups as regards time of onset of infection and duration of life.

Gross areas of myocardial fibrosis occurred with approximately the same frequency and were of about the same degree of severity in each group. There was, in general, sufficient atheromatous change in the arteries themselves to account for the amount of fibrosis present. Certainly, no correlation was apparent in the group with stenotic orifices between the degree of stenosis and the amount of scarring. However, in most cases showing marked stenosis or complete occlusion of the coronary orifices, there was little or no fibrosis either grossly or microscopically. Infarction of the heart in this condition is a relatively rare complication, there being only 3 instances of infarction in this series in which the scarring was due to stenotic coronary orifices. Saphir[24] has reported a similar case of infarction.

CLINICAL FEATURES

The part played by the narrowing or occlusion of the coronary orifices in coloring the clinical picture of luetic aortitis has been subject to much conjecture. There exist no clear-cut criteria at the present time which enable the clinician to make a positive diagnosis. To determine if there were differences in the manifestations of cases of aortic regurgitation with and without stenosis of the coronary openings, the clinical data were compared.

A comparison of these two groups of cases shows that there was a slightly lower age level in the group with stenosed coronary orifices, as indicated in Table V.

TABLE V

RACE, AGE, SEX AND DURATION OF LIFE IN 62 CASES OF SYPHILITIC AORTIC INSUFFICIENCY

		NORMAL CORONARY ORIFICES (28 CASES)	STENOSED CORONARY ORIFICES (34 CASES)
Race	Negro	7	16
	White	20	17
	Yellow	1	1
Sex	Male	23	27
	Female	5	7
Age at time of initial lesion		25.3 yr. (18-38)	23.6 yr. (14-32)
Age at time of cardiac symp.		51.2 yr. (32-69)	46.3 yr. (25-62)
Duration of latent period		22.7 yr. (4-35)	20.5 yr. (5-39)
Time from first cardiac symptom to admission		8.75 mo. (1 wk.-3 yr.)	8.2 mo. (1 wk.-3 yr.)
Time from first cardiac symptom to death		11.4 mo. (1 wk.-3 yr.)	9.9 mo. (2 wk.-3 yr.)
Duration of life from primary lesion		23.4 yr. (4-35)	21.1 yr. (5-39)

The tendency of the colored race to develop cardiovascular syphilis is well known. Not only is the incidence of cardiovascular syphilis high in the negro, but the average age at which he first develops cardiac symptoms is much lower than that for the white. Whether this fact is due to the earlier age at which the negro is infected, or whether it is due to the more rapid and virulent course which the infection runs in this race must remain in doubt, as there were not sufficient data on the latent period of the infection. The ratio of whites to negroes in the total autopsy series in this hospital is about 11:1. In the cases of cardiovascular syphilis, the ratio becomes reduced to 3:1. In the cases of syphilitic involvement of the coronary openings the ratio of negroes to whites is further reduced to 1:1. In other words, approximately 50 per cent of the negroes in the entire series of cardiovascular syphilis (18 out of 37 cases) had partially or completely occluded coronary orifices, as compared to 21.5 per cent of the whites (17 out of 79 cases). This fact may be of some importance in explaining the severity of syphilitic cardiovascular disease in the negro.

TABLE VI

CLASSIFICATION OF CHIEF COMPLAINTS IN 62 CASES OF SYPHILITIC AORTIC INSUFFICIENCY

	NORMAL CORONARY ORIFICES (28 CASES)	STENOSED CORONARY ORIFICES (34 CASES)
Dyspnea	18	20
Orthopnea	2	4
Paroxysmal nocturnal dyspnea	3	0
Pain (cardiac)	10	13
Edema	5	7
Cough	4	3
Weakness	2	6
Insomnia	1	0
No cardiac symptoms	2	4

Chief Complaints.—The chief complaints which brought the patient to the hospital are shown in Table VI. Dyspnea and cardiac pain were much the most common. As can be seen, however, no striking differences exist between the two groups.

TABLE VII

CLASSIFICATION OF SYMPTOMS IN 62 CASES OF SYPHILITIC AORTIC INSUFFICIENCY*

	NORMAL CORONARY ORIFICES (28 CASES)	STENOSED CORONARY ORIFICES (34 CASES)
Dyspnea	26	28
Orthopnea	16	21
Paroxysmal nocturnal dyspnea	9	14
Pain	19	26
Edema	14	11
Cough	17	16
Palpitation	10	12
Weakness	9	10
Choking	2	4
Insomnia	11	9
Hoarseness	3	1

*Two of the cases with normally patent coronary orifices and four of the cases with stenosed orifices presented no cardiac symptoms.

TABLE VIII

CLASSIFICATION OF CARDIAC PAIN IN 40 CASES OF AORTIC INSUFFICIENCY*

	NORMAL CORONARY ORIFICES (16 CASES)	STENOSED CORONARY ORIFICES (24 CASES)
Type—		
Pain (severe, sharp, sticking, etc.)	6	13
Ache (distress, dull, soreness)	2	3
Oppression (squeezing, pressing, smothering)	2	5
Boring	0	1
Location—		
Precordium	5	6
Substernum	5	8
Epigastrium	3	9
Chest	0	0
Radiation—		
l. arm	2	8
r. arm		4
l. shoulder	1	4
r. shoulder		3
neck	0	1
back		3
substernum		3
precordium	1	1
abdomen		1
l. chest	1	
no radiation	1	4
Steady		
Attacks		

*In order to eliminate all cases with pain which might possibly be due to aneurysm, this table includes only cases of uncomplicated syphilitic aortic insufficiency. There were nine cases of aneurysm in the stenosed group and 10 in the group with normal orifices. Furthermore, 2 cases of aortic insufficiency in the normal and 1 case in the stenosed group were not included because of significant arteriosclerosis of the coronary arteries.

When these groups are compared as to total symptoms, there is again great similarity between them (Table VII).

Only minor variations in the frequency of the symptoms occurred. It should be noted with regard to pain that there was the same number of cases with aneurysm in the two groups. The frequency with which cardiac pain is experienced in aortic syphilis has been assumed by Coombs,[7] among others, to be due to obstruction of the coronary orifices.

The clinical charts were incomplete in detail, especially in the earlier years, with respect to the description of cardiac pain. It does appear, however, that pain referred to the epigastrium is twice as common in those cases with coronary orifice occlusion as in the nonaffected group. In those cases with coronary orifice occlusion the pain has a definitely greater tendency to radiate than in the other groups. It is also of interest that cardiac pain was present in 15 cases (62.5 per cent) of the stenosed group in contrast to only 5 cases (27.8 per cent) in the other group. The absence of pain, however, does not rule out the presence of stenosis or occlusion. On the basis of the available data, clinical differentiation between the cases with involvement of the coronary orifices and those without such involvement is often difficult or impossible (Table VIII).

Physical Findings.—A consideration of the chief findings on physical examination is found in Table IX.

TABLE IX

CHANGES ON PHYSICAL EXAMINATION IN 59 CASES OF SYPHILITIC AORTIC INSUFFICIENCY

	NORMAL CORONARY ORIFICES (26 CASES)	STENOSED CORONARY ORIFICES (33 CASES)
Cardiac hypertrophy—		
no enlargement	2	1
slight enlargement	9	18
marked enlargement	15	14
Rhythm—		
regular	17	22
extrasystoles	7	10
Gallop	4	5
Thrill	4	6
Peripheral sclerosis—		
none	2	3
slight	12	19
marked	4	1
Edema—		
none	4	12
slight	15	12
marked	4	7
Hypertension (over 160 systolic or 100 diastolic)	12	11

In addition to these, both groups showed some or all of the well-recognized signs of aortic insufficiency. Practically all the cases in each group showed a Corrigan pulse with a large pulse pressure, as well as the characteristic diastolic murmur. The hearts in the group with normal coronary orifices were usually markedly enlarged, while in the other group they tended to be only slightly enlarged. This finding on physical examination checks with the pathological findings. There was great similarity in the types of heart rhythm between the two groups. There was a slight tendency of the cases with normal coronary openings to show marked peripheral sclerosis, which may possibly be due to the somewhat greater age of these patients. The frequency of hypertension was approximately the same in both groups. Noteworthy, however, is the fact that over twice as many patients with stenosed coronary orifices failed to show edema as did those in the other group.

Roentgen Ray Examination.—No specific change in the x-ray picture can be attributed to syphilitic disease of the coronary orifices. The hearts are smaller in the group with stenotic orifices, but this difference in size is of doubtful diagnostic aid.

Wassermann Reaction.—Table X gives the results of the Wassermann reactions in the two groups. There are no conspicuous differences between them.

TABLE X

SEROLOGY IN 62 CASES OF SYPHILITIC AORTIC INSUFFICIENCY

	NORMAL CORONARY ORIFICES (28 CASES)	STENOSED CORONARY ORIFICES (34 CASES)
Blood Wassermann—		
Strongly positive	25	27
Weakly positive		2
Anticomplementary		1
Negative	2	1
Test not performed	1	3
Spinal fluid—		
Strongly positive	1	4
Negative	2	4

Electrocardiogram.—The electrocardiogram in syphilitic aortitis shows no abnormalities which can be termed characteristic. The commonest finding is left axis deviation, which may well be associated with the hypertrophy of the left ventricle occurring with aortic insufficiency. Juster and Pardee[25] found abnormal T-waves in 85 per cent of 34 cases of aortic insufficiency. They state that "coronary narrowing by luetic aortic aortitis must lead to a defective nutrition of the heart muscle and this we believe is the cause of the abnormalities found in the electrocardiograms of our patient with aortic insufficiency." This opinion is not uncommon.

Electrocardiographic tracings were made in 13 cases with normal or slightly narrowed coronaries and on 12 cases which showed markedly stenosed or occluded coronary orifices (Table XI).

TABLE XI

ELECTROCARDIOGRAPHIC CHANGES IN 25 CASES OF SYPHILITIC AORTIC INSUFFICIENCY*

	NORMAL CORONARY ORIFICES (13 CASES)	STENOSED CORONARY ORIFICES (12 CASES)
Premature beats	3	4
Prolonged A-V conduction	3	2
Right axis deviation	0	1
Left axis deviation	11	8
QRS—		
abnormal duration	3	2
notched or slurred	7	7
low voltage	1	1
Total significant QRS abnormalities	11	10
T-wave—		
down in Lead I	3	5
down in Lead II	1	0
down in Leads I and II	5	4
diphasic in Lead I	1	0
low voltage	3	1
Total significant T-wave abnormalities	13	10
No abnormalities of T-wave	1	3
Bundle-branch block	3	4
Partial heart-block	1	0

*All cases with significant arteriosclerosis of the coronary arteries have been omitted from this table.

No significant differences between the two groups were found. The abnormalities of the T-waves and of the QRS group as well as the frequency of occurrence of left axis deviation were approximately the same in both groups. It appears that abnormalities in electrocardiograms of patients with luetic aortic regurgitation cannot be ascribed solely to coronary orifice stenosis or occlusion.

Clinical Types.—A critical study of the cases with stenosed coronary orifices leads to the impression that one type of case stands out sharply by reason of certain distinctive features. There were 5 such cases in this series (14.7 per cent). They can be segregated roughly by age, but more definitely by the clinical and pathological findings.

1. They were characterized by their youth. All were in the third and fourth decades of life. No case in this series was alive after the age of forty years. The youngest was twenty-one years, the oldest thirty-nine. The average age was 33.6 years.

2. Sex and race were not distinctive.

3. Examination of the hearts showed little or no hypertrophy in the 5 cases of this series. The largest heart weighed 420 gm., the smallest 260 gm. The average weight was 370 gm.

4. Except in one instance, in which large atrophic scars were found, the myocardium was free of gross fibrosis. Histologically, there was a small amount of fine scarring, and two cases showed focal necroses.

5. In no instance was arteriosclerosis of the coronary arteries present. Both coronary orifices were extremely stenosed in 4 cases. The fifth case showed marked stenosis of the left opening and slight narrowing of the right. The right coronary orifice was occluded in two.

6. Pain was the predominant complaint in all. It was paroxysmal in type, being referred in one case to the precordium, in the others to the epigastrium or to the sternum. Radiation of the pain was present in 4 of the 5 cases.

7. The absence of edema in all cases was striking.

8. The average duration of life after the onset of cardiac symptoms was 3.2 months (3 weeks—7 months), as contrasted with 9.9 months (Table IV) for the total group.

The following case histories are illustrative of this group:

CASE 1.—History, No. 361980, D. P., a twenty-one-year-old colored girl, was brought to the admitting clinic at 2 A.M., February 12, 1932. She was obviously in great pain. When seen a few minutes later she was in collapse. She was very pale, pulseless, and no signs of cardiac activity could be elicited. Her respirations became labored, and with each gasp pink froth exuded from her nose and mouth. Emergency measures were ineffectual, and she died within fifteen minutes.

Some history was obtained from her husband. He had known her for seven years and had been married to her for the last three years. Other than an appendectomy in 1925, she had always been well so far as he knew. There had been no rheumatic manifestations. Starting five months before admission, she began to complain of pain in the epigastrium and dyspnea on exertion. She began to use two pillows at night. Three months before admission she had an attack of severe epigastric pain lasting about twenty-four hours, relieved by a hypodermic. For one month she had epigastric pain after meals, relieved by rest. For the last week she had been able to take only fluids because of the distress. Nine hours before admission she had a recurrence of the pain, similar to the attack which she had had three months before. Her physician gave her a fluid medicine, part of which she vomited. He then sent her to the hospital.

Autopsy No. 11,100. There was nothing of interest other than the heart and aorta. The heart weighed 260 grams. The epicardium was smooth. The right auricle, tricuspid valve, right ventricle, pulmonic and mitral valves and left ventricle were normal. The aortic valve flaps were slightly thickened, and the commissures were widened. The left coronary artery arose 1 cm. above the line joining the commissure, the right 2 mm. above. The orifices were almost occluded by the intimal plaques in the aorta, but there was no narrowing or occlusion in the rest of their course.

The myocardium showed no gross fibrosis.

The aorta was elastic and of normal size. Except for longitudinal wrinkling in the ascending portion, it was normal. In the descending portion, particularly the lower half, there were numerous atheromatous plaques which were calcified.

The lungs showed edema.

Microscopically, the heart muscle fibers were of normal size. There were several areas of necrosis in the myocardium, associated with inflammatory reactions.

The accompanying cellular reaction consisted in the main of elongated mononuclear cells resembling fibroblasts, many of which were in a state of mitosis. With them were a few large mononuclear ameboid cells with vacuolated cytoplasm. With the muscle necrosis, there were also a few polymorphonuclears. The blood vessels were normal.

The aorta showed the typical picture of syphilis. There was thickening of the intima with small lymphoid accumulations near the endothelium, penetrating blood vessels in the media with perivascular infiltration of lymphoid and plasma cells. Many of the vasa vasorum had greatly thickened walls.

CASE 2.—History, No. 353635, M. S., a thirty-three-year-old widowed negro housewife, was first seen on September 16, 1932, when she came to the out-patient clinic complaining of acute pain in the epigastrium radiating to both shoulders, both arms and around the heart. She had been married five years before, her husband "dying of insanity" two years later, at the age of thirty-nine years. One baby died soon after birth. The next pregnancy resulted in a miscarriage.

The patient had been perfectly well until five years before, when she married. Almost immediately she developed "womb trouble" with pain in the lower abdomen and leucorrhea. Three weeks before admission, after climbing three flights of stairs she suddenly developed terrific substernal pain which radiated through to the back and to both shoulders and arms. The pain was so bad that she fainted and was unconscious for about eight minutes. When she regained consciousness, she still had some epigastric and substernal discomfort. She stayed in bed for a day, with little relief. Since then she had had recurring attacks while walking, on eating, or on drinking cold water. With these severe attacks of pain, she would break out in a cold sweat and feel faint for a few minutes. She became dyspneic and orthopneic and for three or four nights before admission had had paroxysms of nocturnal dyspnea.

On examination she appeared to be acutely ill, crying out at intervals and holding her hand to the precordial region. The examination was negative except for the cardiovascular system. The heart was slightly enlarged. The left border of dullness was 6 cm. in the second interspace, 8 cm. in the third and 11 cm. in the fifth interspace to the left of the sternum. There were no thrills or shocks. The rhythm was regular. The rate was 80 per minute. The heart sounds were of poor muscular quality. A short systolic murmur and long blowing diastolic murmur were heard at the base in the third left interspace, transmitted over the precordium. The pulse was of the Corrigan type. The peripheral vessels were not sclerotic. The blood pressure was 172/50 in both arms. The liver was not palpable, the lungs were clear, and there was no edema of the extremities.

A leucocyte count showed 6,000 cells with 53 per cent polymorphonuclears and 47 per cent small lymphocytes. A blood Wassermann was not done.

She was immediately admitted to the hospital. Her temperature was 99.3°, pulse 74, respiration 20. While under observation, she had attacks of severe pain coming on every few minutes. Nitroglycerin gave only momentary relief. Morphine gave some relief, but the pain persisted and she began to vomit small amounts of bile-stained fluid. Twelve hours after admission she suddenly stopped breathing.

Autopsy No. 11,050. The pathological findings of interest were confined to the heart and aorta. The heart weighed 400 grams. The epicardium was smooth and glistening. The tricuspid, pulmonic and mitral valves were normal. The aortic valve cusps were thickened and retracted, and their commissures widened. The thickening of the valves was almost entirely confined to the free margins of the cusps. Here there was a rolled, considerably stiffened ridge involving the major portion of the free margin of each cusp. The bases of the cusps were normal.

The root of the aorta, for a distance of 2 cm. above the commissures, was thickened, irregularly wrinkled and contained many shallow pits and depressions. Just above the right posterior cusp of the aortic valve, the aorta was raised over an area 1 cm. in diameter, and beneath this raised area was a small accumulation of yellow material, apparently in the media. The wall about this material was gray and translucent, and beyond was a wide zone of injected vessels. The process in the base of the aorta ended sharply in a wavy line. In the remainder of the aorta, the intima contained many small elevated gray and yellow patches, most marked in the thoracic aorta. No definite longitudinal wrinkling was seen.

The mouths of the coronary arteries were markedly involved and were well above the level of the highest commissure. The right coronary had two pin-point orifices. The left coronary orifice was found to be much larger than the right, but immediately beyond the orifice, the lumen was found to be practically occluded by wrinkled, translucent, thickened intima. The distal portions of both coronaries were normally patent, and contained only a few small atheromatous plaques.

The myocardium was brownish red, firm and free from obvious fibrosis.

Microscopically the muscle fibers were somewhat increased in size. There were a few fine, fibrous scars throughout, and some sections disclosed a beginning necrosis of some of the muscle bundles. In several areas the muscle fibers appeared shrunken and their structure was indistinct. No cellular infiltration could be seen. The smaller vessels appeared to be normal.

These case histories typify that form of luetic coronary orifice involvement which may well be called the acute form of the disease. The process evidently advanced too rapidly to allow the development of an adequate collateral circulation. Clinically, the patients show many of the signs and symptoms of acute coronary obstruction. It is only in this type of case, where there is rapidly progressive narrowing of the coronary orifices, that the diagnosis can be made with any great degree of accuracy.

Mode of Death.—In the presence of aortic insufficiency, the enlarged heart may fail without showing any evidence of myocardial injury other than hypertrophy. It has been argued that partial or complete closure of the coronary orifices may also play an important rôle in producing failure. A number of reports have been published to substantiate this point, among others, those of O'Sullivan[12] and Leary and Wearn.[6] Clawson and Bell[5] noted that 25 patients in their series of 126 died suddenly. Of these, 15 hearts were examined. Closure of the coronary orifices was the conspicuous anatomical change found in all. While there was some hypertrophy (average 403 gm.) "it was not marked and was not of sufficient degree to be responsible for

TABLE XII

MODE OF DEATH IN 62 CASES OF SYPHILITIC AORTIC INSUFFICIENCY

	NORMAL CORONARY ORIFICES (28 CASES)	STENOSED CORONARY ORIFICES (34 CASES)
Gradual failure	6	5
Rapid failure	10	12
Sudden death	12	17

bringing about the sudden death. In these cases, death resulted primarily from the narrowing of the coronary orifices."

An analysis of the manner in which the patients of this series died is shown in Table XII.

There is a slightly greater tendency on the part of those patients with stenosed coronary orifices to die suddenly. There were 5 cases which showed extreme stenosis of both coronary openings (4 mm. or less in circumference), and the average heart weight was 370 gm. All of these patients died suddenly. On the other hand, there were 7 cases in which only one orifice showed extreme narrowing. The average heart weight in these cases was 660 gm. Only three of these individuals died suddenly. It appears that marked stenosis of both coronary orifices predisposes to sudden death.

SUMMARY AND CONCLUSIONS

One hundred and eighteen cases of cardiovascular syphilis have been analyzed to determine the bearing of coronary orifice stenosis upon the pathological and clinical picture of the disease. The degree of orifice involvement was determined by actual measurement. The method of measurement was described. It was found that the normal coronary orifice was about 10 mm. in circumference, the lower limit of normal 8 mm. The pathology and mechanism of occlusion of the coronary openings were discussed. Thirty-nine cases (33 per cent) of the 118 studied showed coronary orifices, one or both, 7 mm. or less in circumference. Of these 39 cases, 34 (87 per cent) had aortic insufficiency. These cases were then compared with 28 which showed aortic insufficiency but with no coronary orifice stenosis. The following observations were made:

1. The right coronary orifice was found to be much more frequently occluded than the left, 8 times to one.

2. An abnormally high origin of the coronary arteries appeared to be an important factor in the involvement of their orifices.

3. On the average, the hearts with stenosed coronary orifices were found to be less hypertrophied than those with patent coronary openings.

4. Infarction was relatively rare in cases with syphilitic stenosis or occlusion of the coronary artery orifices.

5. The clinical data were reviewed. Negroes were much more prone to develop stenosis of the coronary openings than were white people, 48 per cent of the negroes showing this complication as compared to 23 per cent of the white group. There appeared to be a slightly lower age level at which those cases with stenosed orifices had their initial lesions and developed their first cardiac complaints. This was found to be due to the large number of negroes in this group. The duration of life from the onset of cardiac symptoms was shorter in the patients

with stenosed coronary orifices than in the group with patent coronary openings.

6. No major differences were observed between the two groups as regarded symptoms, findings on physical examination or other diagnostic criteria. Electrocardiographic tracings in this condition were briefly discussed.

7. A clinical and pathological picture was drawn, and two cases were reported in full, illustrating the type of case with syphilitic coronary orifice involvement which lends itself most easily to diagnosis.

8. Extreme stenosis of the coronary openings due to syphilis predisposes to sudden death.

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STUDY OF GLUCOSE THERAPY IN HEART FAILURE IN ADVANCED CARDIAC DISEASE*

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DURING the last eight years there have been many reports in the literature concerning the use of glucose in the treatment of cardiac failure. Experimentally there is evidence that the feeding of glucose results in an increase of glycogen in the cardiac muscle. In 1929, Bayliss, Mueller and Starling[1] found that insulin and glucose would prolong the life and efficiency of a heart-lung preparation. A. Valdes[2] in 1929 demonstrated that in fasted rabbits glucose and insulin caused the stores of glycogen in the ventricular muscle to increase in greater proportion than in any other organ or muscle. They drew attention to the possible importance of this fact in treating patients with heart disease. C. N. H. Long and G. T. Evans,[3] 1932, showed that insulin and glucose given together to fasted rats caused a definite increase in glycogen in the heart, as well as in the gastrocnemius muscle. Insulin augmented the effect of glucose in the experience of all three of these groups of investigators.

Clinical evidence in favor of glucose therapy in cardiac disease has been presented by various authors since 1926. At that time there was a report by Osato[4] in which a patient twenty-one years old with mitral stenosis and advanced heart failure was given 50 c.c. of 10 per cent glucose intravenously, with 5 units of insulin subcutaneously. Within half an hour after the injection the patient was relieved of his dyspnea and fell asleep. On the following two days he had a diuresis of 3200 and 4400 c.c. The author remarked that glucose has an "enormous therapeutic power" in severe cardiac insufficiency. In 1927 Stejskal[5] recommended the injection of 20 c.c. of 33 per cent to 50 per cent glucose two or three times weekly in cardiac insufficiency, angina pectoris, pulmonary edema, and a variety of conditions other than cardiac. No insulin was used. No data or case reports are given. Jagic and Klima[6] in 1927 reported definitely good results in treating pulmonary edema, angina pectoris and cardiac dyspnea with 20 c.c. of 40 per cent glucose intravenously. They advise a "small bleeding" before the injection.

In 1928 Smith, Gibson and Ross[7] reported striking improvement in cardiac patients who were given a high carbohydrate diet.

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Kisthinios and Gomez,[8] 1930, report the results of treating cardiac failure with glucose by mouth, together with insulin subcutaneously. They administered 80 grams of glucose in the form of saturated syrup, together with 4 units of insulin. This was given every morning for eight or ten days. Their patients seemed to get temporary relief from nocturnal dyspnea and pulmonary edema.

Rimbaud, Balmès, and Martin[9] (1931) used 50 per cent glucose by mouth, 100 c.c. per day for five days with 5 units of insulin before each dose. After five days the amounts were doubled. They found that dyspnea was relieved very promptly, within the first quarter of an hour; that diuresis began in forty-eight hours and continued with disappearance of edema. There was relief of anginal pains. Visceral stasis was not relieved effectively.

In 1932 Sprague and Camp[10] reported the results of giving from 50 to 100 c.c. of 50 per cent glucose intravenously to a group of 19 patients. In congestive heart failure there was slight effect and no satisfactory diuresis. There was no effect in diphtheritic myocarditis except that the patient was "kept comfortable up to the moment of death." No effect was noted in coronary thrombosis. In two cases of paroxysmal tachycardia there was improvement; in two similar cases, none. They quote Marvin as giving the following indications for glucose therapy in cardiac disease: (1) congestive heart failure not responding to other treatment; (2) diphtheritic myocarditis; (3) coronary thrombosis in which shock is a presenting factor; (4) paroxysmal tachycardia.

The present study was undertaken with a view of determining the scope and value of glucose as an adjunct to other forms of cardiac therapy. It is a report of the use of glucose in 16 cases of heart failure in advanced heart disease. An effort was made to control the observations by keeping the patient at rest without treatment for two or three days before giving glucose. This was not always justifiable in urgent cases, in some of which glucose was given at once, and in others, digitalis. In the latter, glucose was given after the effects of digitalis had been observed. Since all the patients received both glucose and digitalis at different times, it is possible to make some comparison of the effects of the two agents in the same case.

The criteria used to estimate the effect were: first, relief of dyspnea and of pain, both subjectively and objectively; second, diuresis; third, decrease of edema and of evidence of visceral congestion; fourth, the combination of all favorable changes, i.e., restoration of compensation; fifth, any definite improvement in general condition.

Glucose was given in 5, 10, 25, and 50 per cent solutions. On several occasions from 5 to 10 units of insulin were administered fifteen minutes before the glucose. There appeared to be no striking relation of therapeutic results to the concentration of the solution or to the use or

omission of insulin. It was found that 50 per cent glucose tended to produce heavy sweating and occasionally thrombosis of veins near the site of injection. The 25 per cent solution did not cause these inconveniences and was used in the majority of cases.

The cases are presented in chronological order.

CASE 1. The patient was a white man of thirty-one years, whose presenting condition was paroxysmal tachycardia of ventricular origin. He gave a history of an attack suggestive of coronary occlusion one year preceding admission and had had several prolonged attacks of paroxysmal tachycardia during the preceding eleven months. The attack observed on admission had lasted about three weeks. Efforts to stop the attack with quinidine were only temporarily successful, and his dyspnea and weakness progressed to profound prostration with signs of circulatory failure. Four days before death he showed marked venous engorgement and a phlebotomy with removal of 325 c.c. of blood was performed. Immediately following this he was given 50 c.c. of 50 per cent glucose intravenously. The venous stasis and general prostration were slightly improved for a few hours. Heavy sweating followed the glucose injection. In the next four days he developed ascites, massive edema of the legs, and edema of the lungs, and died. At autopsy a localized myocardial scar was found, but no evidence of coronary sclerosis or of valvular disease. The etiology of the original infarction in so young a subject remained obscure. It was impossible to attribute any therapeutic effect to the glucose, other than a transient general support.

CASE 2. A woman forty-eight years old was admitted to the ward with a heart rate of 145, breathlessness, and edema. Auricular fibrillation was present. The liver was engorged and there were râles at the bases of both lungs. The patient had had no digitalis for ten days. After two days' rest in bed there was slight improvement in symptoms and the heart rate was 130. Her heart disease was thought to be due to a toxic thyroid adenoma of long standing. On two successive days she was given 100 c.c. of 5 per cent glucose preceded by 5 units of insulin. On each occasion there was transient subjective lessening of the dyspnea. The heart rate tended to rise, however, and reached 170. The edema increased and the patient gained six and one-half pounds in four days. Glucose administration was discontinued, and she was digitalized with prompt and satisfactory improvement. The edema subsided slowly and she was discharged in good condition. Subsequent observations in the out-patient department have invariably shown rapid auricular fibrillation in spite of the use of digitalis, but no evidence of congestive failure. She has declined treatment for the thyroid condition.

CASE 3. A young man thirty-one years old with a history of high blood pressure for ten years came in with marked dyspnea, orthopnea, and general anasarca. He had been in a hospital for six months and had developed massive edema two weeks before his transfer to our ward. On admission he was given 0.5 gm. of digitalis, and then was observed without medication for two days. His vital capacity was 1151 c.c. His blood pressure was 180/130. The nonprotein nitrogen was 138 mg. per cent. He was given 100 c.c. of 10 per cent glucose preceded by 5 units of insulin. The dyspnea was subjectively less, and he could lie flat. The vital capacity was 1340 c.c. but in three days he had gained four pounds. He was digitalized without effect upon the dyspnea, urine output, or edema. At this point daily injections of 100 c.c. of 50 per cent glucose were started. This produced considerable subjective relief of dyspnea and of general discomfort. The urine output was increased from 1,000 c.c. to 1,500-2,000 c.c. However, he continued to gain weight steadily with increasing anasarca. At the end of two weeks he had gained 15

pounds. Salyrgan intravenously was not effective in producing diuresis. Both the blood pressure and the nonprotein nitrogen rose, and his condition became more and more distressing. He received nine injections of 50 per cent glucose, this being the only form of therapy that seemed to yield any benefit. Each dose gave transient relief of dyspnea and general discomfort and tended to quiet restlessness, and also to improve the patient's mental outlook. In fact, there was a certain euphoria following each injection. The available veins became thrombosed, and intravenous therapy had to be given up. The patient became moribund and died ten days later. Autopsy showed chronic glomerular nephritis and cardiac hypertrophy.

CASE 4. A man, aged fifty-five years, who was definitely senile came into the ward a few hours after an early morning attack of precordial pain and dyspnea. He had had a similar attack followed by the onset of congestive failure nine months previously. On admission his blood pressure was 200/125 with pulsus alternans. Numerous râles were heard at the bases, the liver was slightly enlarged, and there was slight edema of the ankles. The electrocardiogram showed T-waves of the "coronary" type. He was observed at rest for three days. His dyspnea tended to be less and the edema of the feet disappeared, but later the dyspnea returned with cough. He was given 100 c.c. of 10 per cent glucose preceded by five units of insulin in the evening. The next day he volunteered the information that his shortness of breath and cough had been greatly relieved following the injection and that he had had a comfortable night. He looked better and was not dyspneic. The next day he developed severe substernal pain following slight exertion. He was seen to be in great distress, with yellowish pallor and cold sweat. One hundred c.c. of 10 per cent glucose with 5 units of insulin were given intravenously. During the administration he obtained relief, and his appearance improved dramatically as his color changed from yellow to a normal shade. He remarked that although the substernal pain was gone he could still feel residual pain in his elbows. Some hours later during the night the substernal pain and dyspnea returned. The next day he was again given 100 c.c. of 10 per cent glucose with 5 units of insulin which was followed by only partial relief, and did not prevent the necessity of using morphine. Administration of digitalis was then started. The following day he looked worse, and the blood pressure had dropped to 130/100. He became drowsy and unresponsive. At 4 P.M. he was given 50 c.c. of 50 per cent glucose. The following morning he reported feeling much better, and was alert and ate well, but looked pale and exhausted. He gradually declined and began to accumulate fluid. Digitalis had no effect. He became comatose and developed embolic gangrene of the left foot and died eight days after the last injection of glucose. Permission for autopsy was not obtained.

CASE 5. A colored man, thirty-one years old, with syphilitic aortic regurgitation had had dyspnea for one month and edema for two weeks. Nocturnal dypnea was severe and was accompanied by distressing cough with blood-streaked sputum. At the time of a nocturnal attack he was given 100 c.c. of 50 per cent glucose with 10 units of insulin. This was followed by nausea and sweating, but there was definite relief of dyspnea for the rest of the night. Following a second dose on the next night there was no sickness, and dyspnea was again relieved. However, the arm veins became thrombosed. There was no diuresis, but the edema of the legs had disappeared. He was then digitalized, and there was some diuresis and partial improvement. Tubercle bacilli were found in the sputum, and he was transferred to a sanitarium.

CASE 6. A fifty-year-old negro had hypertension and uremia. His chief symptom was severe dyspnea. He was given 200 c.c. of 25 per cent glucose on two successive nights with relief of dyspnea for the night. He died a few days later. No autopsy was performed.

CASE 7. A colored woman, aged fifty years, with dyspnea and orthopnea, had a blood pressure of 276/160. There were râles at the lung bases and slight edema. She had been digitalized in the out-patient department before admission. She was given 100 c.c. of 25 per cent glucose on one occasion, from which there was no notable effect. She improved greatly while at rest and her blood pressure declined. On discharge it was 190/120.

CASE 8. A white woman, sixty-nine years old, who was known to have had hypertension for eight years, had suffered three breaks in compensation during the preceding ten months. She had been digitalized to the point of nausea ten days before admission and had received no digitalis since then. She was dyspneic, cyanotic, and orthopneic. There was massive edema. She was given 100 c.c. of 25 per cent glucose the day of admission and again the following night. There was no subjective or objective improvement, but the edema and weakness increased. She was digitalized again without improvement. She was then given salyrgan on two occasions with slight diuresis, 1300 c.c. She was discharged against advice.

CASE 9. A white woman, aged 50 years, with syphilitic aortic regurgitation was admitted to the ward, having gradually become worse upon digitalis therapy. She was digitalized to the point of minor toxic manifestations at the time of admission. She was orthopneic, had numerous râles and considerable pitting edema. She was given 100 c.c. of 25 per cent glucose, which she said was followed by a feeling of oppression in the chest, and restlessness. No immediate improvement was noted. She gradually improved on rest in bed, and the edema and orthopnea disappeared. She had practically no cardiac reserve at the time of discharge.

CASE 10. A negress thirty-four years old had syphilis of three years' standing. She had developed severe anginal attacks with dyspnea. There was no evidence of aortic insufficiency. For one week before admission she had constant dyspnea and swelling of the ankles. During an anginal attack shortly after admission she was given 100 c.c. of 25 per cent glucose with relief of pain and dyspnea. The following day the same result was obtained. She was free from attacks for three days, but on the fourth she had a severe attack of angina from which only partial relief was obtained from glucose. This was followed by an extremely severe attack two hours later. This attack and subsequent ones were promptly relieved by amyl nitrite or by nitroglycerin. Digitalis failed to abolish the attacks either of pain or of dyspnea.

CASE 11. A colored man of twenty-three years had a febrile illness in June, 1932, followed by progressive swelling of the legs and abdomen together with dyspnea and orthopnea. His condition appeared urgent on admission in December, 1932, and he was given 0.6 gm. of digitalis at 11 A.M. At 2 P.M. he was given 50 c.c. of glucose. When seen one-half hour later he was having marked respiratory distress. He began to improve in about an hour and by 5 P.M. was quite comfortable. Continued digitalization was followed by diuresis and complete disappearance of dyspnea and of congestive failure.

No signs of organic heart disease were made out upon physical examination, and the diagnosis was uncertain. Tuberculous peritonitis and tuberculous pericarditis with adherent pericardium were considered. In estimating the effect of glucose, it is notable that the improvement in dyspnea was considerably later than that usually experienced, which is during or immediately after the injection. It is possible that the change in condition at 5 P.M. was due to the digitalis (0.6 gm.) given at 11 A.M. This is borne out by his progressive and lasting improvement on continued digitalization.

CASE 12. A white man sixty-eight years old had arteriosclerotic heart disease with auricular fibrillation. On continued digitalis dosage, compensation was barely

maintained. He developed bronchopneumonia and did poorly, though heart failure was not a conspicuous feature until near the end. At a time when he appeared moribund, he was given 100 c.c. of 25 per cent glucose intravenously with decided improvement in general condition. He died five days later.

CASE 13. A colored male thirty-nine years old had syphilis with aortic regurgitation. A loud musical diastolic murmur suggested a ruptured aortic cusp. He did not do well on digitalis and was admitted to the hospital with progressive failure. There was marked respiratory distress. On two nights he was given respectively 125 c.c. and 200 c.c. of 25 per cent glucose intravenously. This was followed by relief of his distressing dyspnea for hours so that he could rest. At the same time the edema increased, and he became progressively worse and died. No autopsy was obtained.

CASE 14. A white man sixty-five years old had arteriosclerotic heart disease. Decompensation had begun six months previous to admission. Five days before admission he had a "clamping pain" in the chest and epigastrium. He was badly decompensated with orthopnea, cyanosis, massive edema and enlarged liver. He had a moderate fever and a leucocyte count of 11,800. He was given 100 c.c. of 25 per cent glucose. No improvement was observed. Digitalis also had no effect. Oxygen gave some relief of dyspnea. The patient died. A large infarct of the myocardium was found at necropsy.

CASE 15. A patient fifty-five years old, white, male, had evidence of both rheumatic and arteriosclerotic heart disease. The electrocardiogram showed auricular fibrillation and was indicative of profound myocardial damage. He showed râles at both bases, marked engorgement of the liver and slight jaundice. There was moderate edema of the legs. Urgent dyspnea was not manifest. One hundred c.c. of 25 per cent glucose with 5 units of insulin were given on three occasions. No improvement was noted. No diuresis resulted. He was discharged against advice and died within a week.

CASE 16. A white man forty-two years old with mitral stenosis was subject to attacks of cardiac asthma. Shortly after admission he developed an extremely severe attack of dyspnea of an asthmatic type which threatened to prove fatal. He was cyanotic and there was a respiratory effort with stridor. The lungs, however, remained clear, and pulmonary edema did not develop. The patient became unconscious. He was given morphine and atrophine without apparent relief. The morphine seemed to depress further the insufficient ventilation. He was put in an oxygen tent, which caused the cyanosis to clear up, but not the dyspnea and stridor. He was given 100 c.c. of 25 per cent glucose without apparent effect except that the pulse volume, which was small and failing, increased. Immediately following the glucose he was given 6 c.c. of digifolin intravenously. The circulation was supported by giving 1 minim of adrenalin intravenously every five minutes for five doses. About forty-five minutes after the intravenous digifolin, there was some improvement, and the violent dyspnea gradually passed off. Four more cubic centimeters of digifolin were given later in the day. It was thought that the improvement was due to the digifolin, the other measures possibly having served to support the patient through the critical period. This interpretation was suggested by the subsequent course. After the attack just described the patient received no further digitalis, and his dyspnea began gradually to increase three or four days later. One week after the attack he had another which duplicated the first. He was treated again with oxygen, glucose and digifolin intravenously with similar results. Thereafter he was kept on digitalis with steady improvement. There were no further attacks, and he was discharged in a fair state of compensation.

DISCUSSION

In many of the articles referred to earlier in this paper the prompt and dramatic relief of dyspnea following glucose injection or ingestion is emphasized. Relaxation and drowsiness are also mentioned, and in some cases diuresis was observed.

Of our sixteen cases of advanced heart disease with failure we noted definite lessening of the dyspnea in nine. The results were "dramatic" only in one case, Case 4. Five patients who had been restless from dyspnea got considerable relief and were able to sleep. In the other three cases relief of dyspnea was only slight, and in two of these the most notable result was improvement in general condition. In all nine the effect was temporary, lasting from three to twelve hours. Of this group five died and two left the hospital in critical condition. One did well on nitroglycerin. No progressive or lasting improvement was seen. On the contrary there was a tendency for succeeding injections to be less effective. The same statements hold true for the relief of pain of cardiac origin. There was no definite diuresis following glucose injection, even though hypertonic solutions were used. On the contrary, edema and weight were often seen to increase during glucose administration. This series includes no instances of the effect of intravenous glucose on acute pulmonary edema.

Comparison of the Effects of Glucose and Digitalis.—From the above it is apparent that in no case was glucose therapy instrumental in restoring compensation. In three cases, on the other hand, compensation was restored and maintained for an indefinite time by digitalis. These were a case of thyroid heart disease with auricular fibrillation, a case of probable tuberculous pericarditis, and a case of rheumatic heart disease with mitral stenosis. In the first two glucose had no favorable effect. In the third it probably was useful as an emergency measure. In one case of syphilitic heart disease in which there was slight improvement by digitalis, temporary relief of dyspnea was noted from glucose.

Five of the patients were not improved either by digitalis or by glucose. These cases included one of arteriosclerotic heart disease, one of coronary occlusion, one of syphilitic aortic regurgitation, one of rheumatic heart disease, and one of hypertensive heart disease. Three patients died. Two of them, one with hypertensive heart disease and one with syphilitic aortic regurgitation, were improved on bed rest so that they could be discharged. Both were complete cardiac invalids.

The mechanism by which intravenous glucose or glucose by mouth could relieve cardiac dyspnea is not entirely clear. The contraction of cardiac muscle depends not only upon oxygen but also upon carbohydrate, the supply of which theoretically may become precarious in ill-nourished states, thyrotoxicosis and probably coronary disease. The experimental work already mentioned indicated that an increased

TABLE I

RESULTS OF TREATMENT WITH GLUCOSE AND WITH DIGITALIS IN SIXTEEN CASES OF HEART FAILURE IN ADVANCED CARDIAC DISEASE

CASE NO.	AGE	DIAGNOSIS	GLUCOSE					DIGITALIS					ULTIMATE RESULT
			RELIEF OF DYSPNEA	RELIEF OF PAIN	DIURESIS	IMPROVED COMPENSATION	GENERAL IMPROVEMENT	RELIEF OF DYSPNEA	RELIEF OF PAIN	DIURESIS	IMPROVED COMPENSATION	GENERAL IMPROVEMENT	
1	31	Ventricular paroxysmal tachycardia. Congestive failure.	No		Increased edema	No	Yes	No		No	No	No	Died
2	48	Thyrotoxic heart disease. Congestive failure.	Yes		Increased edema	No	No	Yes		Yes	Yes		Discharged. Compensation restored.
3	31	Chronic nephritis and hypertension. Congestive failure.	Yes		Increased edema	No	Yes	No		No	No	No	Died
4	66	Coronary occlusion. Congestive failure.	Yes	Yes	Increased edema	No	Yes	No	No	No	No	No	Died
5	31	Syphilitic aortic regurgitation. Congestive failure.	Yes		No	No	No	Yes		Yes	No	Yes	Discharged to sanitarium.
6	50	Uremia. Hypertension.	Yes		No	No	No	No		No	No	No	Died
7	50	Hypertension. Congestive failure.	No		No	No	No	No		No	No	No	Improved on rest. Discharged.
8	69	Hypertension. Congestive failure.	No	No	Increased edema	No	No	No		No	No	No	Discharged against advice.
9	50	Syphilitic aortic regurgitation. Congestive failure.	No		No	No	No	No		No	No	No	Improved on rest. Discharged.
10	34	Syphilitic aortitis—anginal syndrome. Congestive failure.	Yes	Yes	No	No	No	No	No	No	No	No	Relieved by nitroglycerin. Discharged.
11	23	? tuberculous pericarditis. Congestive failure.	No		No	No	No	Yes		Yes	Yes		Compensation restored. Discharged.
12	68	Arteriosclerotic heart disease. Congestive failure. Bronchopneumonia.	No		No	No	Yes	No		No	No	No	Died
13	39	Syphilitic aortic regurgitation. Congestive failure.	Yes	Yes	Increased edema	No	No	No	No	No	No	No	Died
14	65	Coronary occlusion. Congestive failure.	No	No	No	No	No	No	No	No	No	No	Died
15	55	Rheumatic heart. Mitral stenosis. Congestive failure.	No		No	No	No	No		No	No	No	Died
16	42	Rheumatic heart. Mitral stenosis. "Cardiac asthma."	No		No	No	Yes	Yes		Yes	Yes		Compensation restored. Discharged.

supply of carbohydrate prolongs the life of the heart, augments the glycogen in the heart muscle and increases the efficiency of the musculature. On the basis of these experiments, it is thought that glucose furnishes to the exhausted heart muscle a temporarily increased supply of carbohydrate which may be stored or burned immediately, and which may have a beneficial effect on the entire circulation, including that of the respiratory center. Increased efficiency of the heart muscle would diminish the concentration of carbon dioxide and lactic acid, both of which are powerful respiratory stimulants and which tend to accumulate in the body during cardiac decompensation.

In giving from 25 to 50 grams of carbohydrate intravenously, it is evident that the increased glucose supply is of short duration and that the direct effect upon metabolism is transient. It seems that by forcing carbohydrate feeding over a longer period it might be possible to increase glycogen reserves with more lasting benefit. The results of this method, used by the authors of papers 3, 8, and 9 of the bibliography, are encouraging. However, it would appear doubtful whether daily feeding of concentrated syrups could be borne for very long, especially by patients with impairment of digestive function.

The addition of insulin seems of doubtful value in nondiabetic subjects. The amounts recommended, 5 to 10 units, would appear to be too small to cover the glucose. Moreover, larger amounts of insulin may be of some danger to patients with degenerative heart disease, especially to those with coronary disease and angina pectoris.

In our series it was noted that successive doses of glucose tended to have less effect, and after the effect of glucose had worn off the patients seemed to be worse rather than better. This may have been due to the fact that in most cases the disease was progressing to a fatal termination, but the impression was that there was exhaustion following the period of increased efficiency. Thus glucose may perhaps be classed with cardiac stimulants which increase the action temporarily and may seem to exhaust the heart in so doing. Like such drugs glucose may be most suitable to use in emergencies in which myocardial damage is slight or absent, in order to tide over a critical period, giving time for the organism to readjust itself, recuperate, or take benefit from other measures. It might at times serve to break a "vicious cycle." This suggests itself as a possible explanation of the brilliant result experienced in Osato's first trial of the method. In the same way it may be tried as a means of relief in cases of heart failure at the terminal stage, when other measures are of no avail. It may afford comfort for a time when other measures fail, and so supplement or supplant morphine. In cases of advanced chronic heart disease with congestive failure, our results indicate that intravenous glucose is not effective in restoring or maintaining compensation.

SUMMARY

1. Reports are given of sixteen cases of heart failure in advanced heart disease in which opportunity was afforded for comparison of the effects of glucose and digitalis.

2. In nine cases dyspnea was relieved to some extent. The effect, however, was of short duration (from three to twelve hours) as compared with the more lasting effect of digitalis.

3. Glucose failed to restore compensation in any case. Digitalis restored compensation in three cases.

4. The first injection of glucose seemed to have more beneficial effect than repetitions of the treatment.

5. According to the results of this study glucose therapy appears to be indicated as an emergency measure in cases of acute or urgent heart failure and in cases of advanced chronic heart failure in which digitalis in adequate amounts has not restored compensation.

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ELECTROCARDIOGRAMS THAT REPRESENT THE POTENTIAL VARIATIONS OF A SINGLE ELECTRODE*†

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INTRODUCTION

IN STUDYING the electrical field produced by the heartbeat under various circumstances, we have frequently made use of precordial leads, pad leads, and direct leads in animal experiments, and of precordial leads in clinical investigations.[1, 2] In taking these special leads one electrode (the indifferent electrode) is placed upon one of the extremities,‡ and the other (the exploring electrode) upon the precordium, upon a large gauze pad soaked in saline and laid upon the exposed heart, or directly upon the exposed heart as the case might be. In direct leads taken in this way the potential of the exploring electrode fluctuates through so wide a range in comparison with that of the indifferent electrode that no material error is made if the potential of the latter is regarded as constant throughout the cardiac cycle. In pad leads, and particularly in precordial leads, the potential variations of the indifferent electrode, although no greater in absolute magnitude than in direct leads, are much larger in comparison with those of the exploring electrode, and play a considerably greater rôle in determining the form of the curve recorded. In standard leads the two electrodes are approximately equidistant from the heart; on the average their potential variations are of about the same magnitude and influence the form of the electrocardiogram in equal measure.

In general the curves obtained by means of the special leads mentioned are more or less helpful in solving electrocardiographic problems in proportion to the amount of information that can be gained by comparing the deflections of one lead with those inscribed in another during the same phase of the cardiac cycle. The deflections of pad leads and precordial leads are compared with each other and with the corresponding deflections of direct and standard leads. The analysis depends in the main upon the discovery of similarities, of deflections that are alike in form and correspond in time. Differences between the leads compared with respect to the relative magnitude of the potential variations of the

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‡It has usually been placed upon the left leg in taking clinical curves and upon the left hind leg in animal experiments.

two electrodes tend to obscure these similarities and often make the interpretation of the curves difficult. In order to obtain deflections of similar size the string galvanometer must be made approximately ten times as sensitive when taking precordial as when taking direct leads. Deflections due to variations in the potential of the indifferent electrode are therefore ten times as large and ten times as conspicuous in the former as in the latter. The differences between direct and standard leads are even greater, and the principles followed in the interpretation of the curves obtained by means of the one cannot be applied to those obtained by means of the other.

In order to overcome these difficulties we have devised leads that record the potential variations of a single electrode. It is the purpose of this article to explain the methods adopted to achieve this end and to show that when they are followed the potential variations of the indifferent electrode are negligible.

METHODS AND APPARATUS

The method of leading referred to is illustrated in Fig. 1. Electrodes are placed upon the right arm, left arm, and left leg, in exactly the same manner as in taking

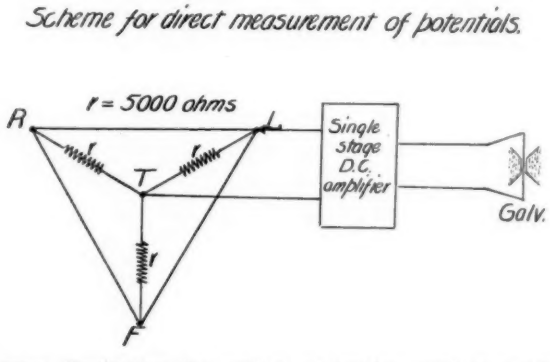

Fig. 1.—Diagram illustrating the method of leading used to record the potential variations of a single electrode. Electrodes on the right arm (*R*), left arm (*L*), and left leg (*F*) are connected through equal resistances of 5,000 ohms to a central terminal (*T*). The central terminal and an exploring electrode, or one of the extremity electrodes as indicated here, are connected to the input terminals of a vacuum-tube amplifier with a balanced plate circuit in which the string galvanometer is inserted.

the three standard leads. They are connected, each through a separate noninductive resistance (*r*), to a central terminal. The three resistances used must be equal and should be large in comparison with the largest body resistance between any two of the three electrodes. In our earliest experiments we employed resistances of 25,000 ohms, but this made our apparatus so sensitive to stray alternating currents that resistances of 5,000 ohms were finally substituted. These greatly reduced the amount of stray current picked up, and proved to be reasonably satisfactory if the skin resistance was kept sufficiently low. The central terminal serves as the indifferent electrode, and we shall show that its potential is not materially affected by the heart's electrical field. The exploring electrode may be placed upon the precordium or upon any other part of the body whose potential variations are to be

recorded. Leads from each of the extremity electrodes in succession to the central terminal are used to obtain the potential variations of the right arm, left arm, and left leg.

The central terminal and the exploring electrode are connected to the input terminals of a vacuum tube with a balanced plate circuit.* The string galvanometer is joined to the plate circuit in such a way as to include a variable resistance and a portion of the plate battery between its terminals. The value of the resistance is so adjusted that the drop in potential across it due to the plate current when the input terminals of the tube are shortcircuited is exactly balanced by the voltage drop in the included portion of the battery. When the plate current changes in response to a change in the potential of the grid with respect to that of the filament, this balance is disturbed and a small fraction of the plate current flows through the string galvanometer.

One of the chief advantages of this arrangement is the very high resistance in the input circuit. The addition of twenty-five, fifty, or even one hundred thousand ohms to the resistance in this circuit does not appreciably alter the size of the string deflection produced when an electromotive force of one millivolt is thrown into it. The tension of the string is adjusted to give the proper sensitivity at the beginning of a set of observations and usually does not need to be changed thereafter. No overshooting, due to the condensor-like effect of the skin, occurs when the skin resistance is high. The flow of current in the input circuit is so small that electrodes of almost any type can be used without fear of polarization effects. Since practically no current flows, the potential differences that it is desired to measure are not altered. The chief disadvantage lies in the difficulty of avoiding interference by stray alternating current. This is much greater than when the string galvanometer is used in the ordinary way, and it increases rapidly with an increase in the external† resistance of the input circuit.

POTENTIAL OF THE CENTRAL TERMINAL

At any instant the sum of the differences in potential between the central terminal and any three electrodes connected to it is zero. The mean potential of these electrodes and the potential of the central terminal are equal. To prove these statements, let V_T represent the potential of the central terminal, and r the magnitude of the equal resistances through which it is joined to three electrodes in contact with the body. If the potentials of the three electrodes are represented by V_A, V_B, and V_C and the currents flowing from these electrodes toward the central terminal by I_A, I_B, and I_C, respectively, these quantities must satisfy the following equations:

$$V_A - V_T = rI_A \quad (1)$$

$$V_B - V_T = rI_B \quad (2)$$

$$V_C - V_T = rI_C \quad (3)$$

By adding these equations we obtain

$$(V_A - V_T) + (V_B - V_T) + (V_C - V_T) = r\,(I_A + I_B + I_C) \quad (4)$$

*The circuit we are using is essentially the same as that employed in Dr. W. J. V. Osterhout's laboratory at the Rockefeller Institute for Medical Research. We wish to thank Dr. Osterhout and his associate, Dr. S. E. Hill, for supplying us with a diagram of this circuit and with the data necessary for its construction.

†Resistance external to the vacuum tube.

The right-hand side of this equation is clearly zero by Kirchkoff's first law, which states that the algebraic sum of all the currents meeting at any point of a network is zero. Consequently,

$$(V_A - V_T) + (V_B - V_T) + (V_C - V_T) = 0 \qquad (5)$$

or

$$V_T = \tfrac{1}{3}\,(V_A + V_B + V_C) \qquad (6)$$

The same method may be used to show that if the central terminal is joined through like resistances to any number of electrodes in contact with the body, the sum of the differences in potential between it and these electrodes must be zero, and the potential of the terminal must be equal to the mean potential of the electrodes.

The difference in potential between the central terminal and any one of three electrodes connected to it may be expressed in terms of the differences in potential between that electrode and the other two. If the electrodes are placed upon the right arm, left arm, and left leg, the difference in potential between the central terminal and the leg electrode, for example, is at all times one-third the sum of the differences in potential between this electrode and the electrodes on the two arms. We may write

$$(V_C - V_T) + (V_T - V_A) = V_C - V_A \qquad (7)$$

$$(V_C - V_T) + (V_T - V_B) = V_C - V_B \qquad (8)$$

By equation (5)

$$V_C - V_T = (V_T - V_A) + (V_T - V_B) \qquad (9)$$

If we substitute e_b for $V_C - V_A$ and e_c for $V_C - V_B$ the addition of equations (7) and (8) gives

$$V_C - V_T = \frac{e_b + e_c}{3} \qquad (10)$$

In the same way it may be shown that if e_a is substituted for $V_B - V_A$

$$V_A - V_T = -\frac{e_a + e_b}{3} \qquad (11)$$

and

$$V_B - V_T = \frac{e_a - e_c}{3} \qquad (12)$$

In deriving the foregoing equations (1 to 12 inclusive) we have made no assumptions of any kind. It should be noted, however, that the symbols V_A, V_B and V_C appearing in these equations represent the potentials of the three electrodes in contact with the body after these electrodes have been connected to the central terminal. We desire to study the electrical field produced by the heart under natural conditions, and we must take care that our method of measurement does not modify to a material extent the quantities that we wish to measure. The heart's electrical field must be altered by any procedure that changes the resistance between points that are at different potentials. Changes in re-

sistance between points at the same potential have, of course, no effect upon the flow of current. The effects produced by attaching electrodes to the body surface must vary directly with the size and conductivity of the electrodes, and inversely with their distances from the heart; the effect of connecting these electrodes to a central terminal must vary inversely with the magnitude of the resistances used for this purpose. The extremities may be regarded as linear conductors attached to the trunk; between points on the same extremity there are no differences in potential of cardiac origin that can be detected by measurements made with the string galvanometer at the usual sensitivity. The potentials of the extremities are not, therefore, appreciably altered by placing even large electrodes upon them. The effect of connecting these electrodes to a central terminal may be neglected, if this procedure does not significantly change the potential difference between any two of them during any phase of the cardiac cycle. It will be seen that if we place our three electrodes upon the right arm, left arm, and left leg, and make the resistance r so large that connecting them to the central terminal does not materially alter the size of the deflections in the three standard leads, we shall make no serious error if we treat V_A, V_B, and V_C as if they were the potentials of these extremities before the attachment of the electrodes, and regard e_a, e_b, and e_c as the deflections in the three standard leads. It is clear that to accomplish our purpose we must make r large in comparison with the largest body resistance between any two of the three extremities. A large part of the resistance between one extremity and another is due to the resistance of the skin beneath the electrodes, and if this is kept low r may be made smaller than would otherwise be the case. It will be observed that the resistance of the skin beneath a given electrode is a part of the resistance between the subcutaneous tissues and the central terminal. When the electrodes are placed on the right arm, left arm and left leg, the resistances between this terminal and the apices of Einthoven's triangle, which are represented by the junctions of these extremities with the trunk, cannot be regarded as even approximately equal unless r is large in comparison with the skin resistance or unless the skin resistance is the same beneath all three electrodes. In practice, however, we shall know that r is large enough for our purpose if the curves taken by means of the three standard leads before and those taken in the same way after connecting the extremity electrodes to the central terminal are not significantly different.

DEDUCTIONS BASED ON EINTHOVEN'S TRIANGLE

In a previous publication[3] it has been shown that if the assumptions upon which Einthoven's triangle is based are valid, the potential of the

right arm (V_R), the potential of the left arm (V_L) and the potential of the left leg (V_F) at a given instant are defined by the equations

$$V_R = -\frac{e_1 + e_2}{3} \tag{13}$$

$$V_L = \frac{e_1 - e_3}{3} \tag{14}$$

and

$$V_F = \frac{e_2 + e_3}{3} \tag{15}$$

in which the deflections in standard Leads I, II, and III at the chosen instant are represented by e_1, e_2, and e_3, respectively. It will be seen that at every instant

$$V_R + V_L + V_F = 0. \tag{16}$$

It should be pointed out that the derivation of these equations involves the assumption that an electromotive force generated by the heart and having a direction perpendicular to the plane of the three standard leads will not affect the potential of the right arm, left arm, or left leg. This is equivalent to the assumption that the heart lies in the plane of Einthoven's triangle.

If electrodes on the right arm, left arm, and left leg are connected to a central terminal through like and sufficiently large resistances, we may substitute V_R, V_L, and V_F, for V_A, V_B, and V_C, respectively, in any of the equations in which the latter occur. It is therefore evident from equations (6) and (16) that under the circumstances specified we may, without serious error, regard the central terminal as at zero potential throughout the cardiac cycle. By connecting one of the input terminals of the apparatus, described on a preceding page, to the central terminal and the other to the right-arm, left-arm, and left-leg electrodes in succession we obtain three curves, each of which represents the potential variations of a single extremity. We may designate these curves, which are so taken that relative negativity of the extremity electrode produces an upward deflection in the finished record, by V_R, V_L, and V_F, respectively, and we shall refer to them collectively as extremity potentials. At any instant the sum of the deflections in the right-arm, left-arm, and left-leg leads must be zero. The position of the electrical axis may be determined by means of the formula

$$\tan a = \frac{\sqrt{3}\, V_F}{V_L - V_R} \tag{17}$$

in which a is the angle made by the electrical axis with that side of Einthoven's triangle which corresponds to standard Lead I. The curves obtained by leading from the central terminal to an exploring electrode in contact with the exposed heart, with a pad of gauze laid upon the exposed heart, or with the precordium represent the potential variations of the exploring electrode, and may be referred to as direct, pad,

and precordial potentials, respectively. The symbols V_1, V_2, V_3, etc., will ordinarily be used to designate such curves.

EXPERIMENTS ON A MODEL

In order to test the conceptions at which we have arrived under conditions resembling those postulated as closely as possible, we have carried out a few experiments on a model. An equilateral triangle with sides 12.7 cm. in length was marked out on the bottom of a large shallow galvanized pan measuring 48.3 by 40.6 cm. Electrodes were placed at the apices of the triangle, and two electrodes were placed close together near its center. These central electrodes were 10 mm. apart and were so arranged that the center of the triangle was midway be-

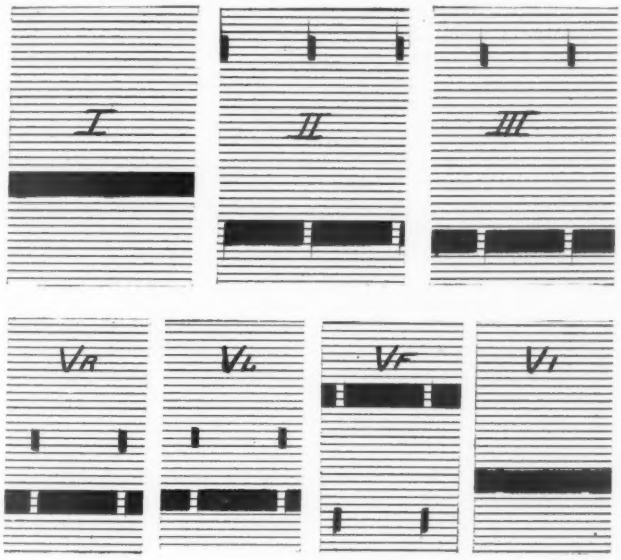

Fig. 2.—Records obtained in an experiment on a model (experiment 2, Table 1). A deflection of 0.5 cm. equals one millivolt. V_1 shows the potential difference between the central terminal and a point equidistant from the central electrodes (see text) and 24 cm. from the center of the triangle.

tween them. After the pan had been filled to a depth of 38 mm. with a weak solution (about 1 per cent) of copper chloride, they were connected to a 45 volt battery through a rotating circuit breaker, which closed the circuit momentarily with each revolution. The apical electrodes were joined to a central terminal through resistances of 5,000 ohms, and the potential variations of these electrodes (V_R, V_L, and V_F) were recorded by connecting the central terminal and each of them in succession to the input terminals of the vacuum tube amplifier previously described (Fig. 2). The three leads corresponding to the three standard electrocardiographic leads were taken with the same instrument, in some instances both before and after connecting the apical electrodes to the central terminal. The potential of the central terminal was also

compared with that of points distant from the center of the triangle and equidistant from the two central electrodes; points which, theoretically, should be at zero potential. The difference in potential between such points and the central terminal was always very small.

TABLE I

EXPERIMENT	ANGLE α. † DEGREES	LEAD I	LEAD II	LEAD III	V_R	V_L	V_F	CENTRAL TERMINAL-DISTANT POINT
1a*	60	32.0	61.0	28.0				
1b	60	31.0	59.0	27.4	−30.0	2.0	28.5	2.0
2	90	0.2	49.0	49.0	−16.0	−16.5	32.6	0.4

Note.—The measurements given above are in tenths of a millivolt.

*In this experiment Leads I, II, and III were taken before (1a) and again after (1b) connecting the apical electrodes to the central terminal.

†The angle between the line joining the central electrodes and that side of the triangle corresponding to standard Lead I.

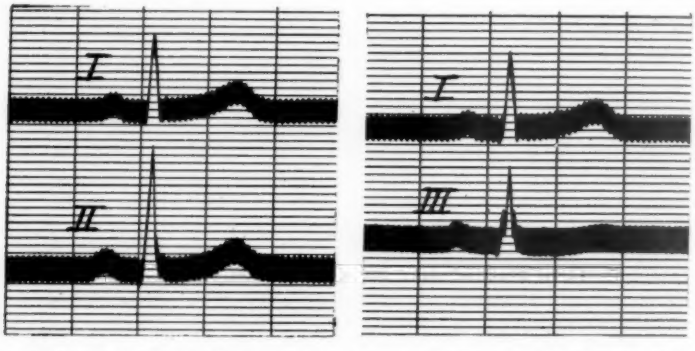

Fig. 3.—Standard electrocardiogram of a normal subject. *QRS* interval, 0.063 second.

The results of two experiments are shown in Table I. In the first the electrical axis was parallel to that side of the triangle corresponding to standard Lead II, and in the second it was perpendicular to the side corresponding to standard Lead I (Fig. 2). The last column of the table gives the difference in potential between the central terminal and a point near the edge of the pan and on the perpendicular bisector of the line joining the two central electrodes. In the first experiment this point was 20 cm. and in the second 24 cm. from the center of the triangle. It will be noted that the potential differences in Leads I, II, and III were somewhat greater before (1a) than after (1b) the apical electrodes were connected to the central terminal. The results of both experiments are in good agreement with the theoretical predictions based on the equations given on preceding pages.

CLINICAL CURVES

We hope in the near future to describe in considerable detail the curves obtained under various circumstances when the method of leading described in this article is employed. We shall therefore confine our

remarks here to a single illustration. The standard electrocardiograms of a normal subject are shown in Fig. 3, and the extremity and precordial potentials of the same subject in Fig. 4. It should be remembered that in the latter curves a negative variation in potential is represented by an upward, a positive variation in potential by a downward deflection of the string shadow. The curves obtained from the right side of the precordium (V_1, V_2, and V_E) show a small downward

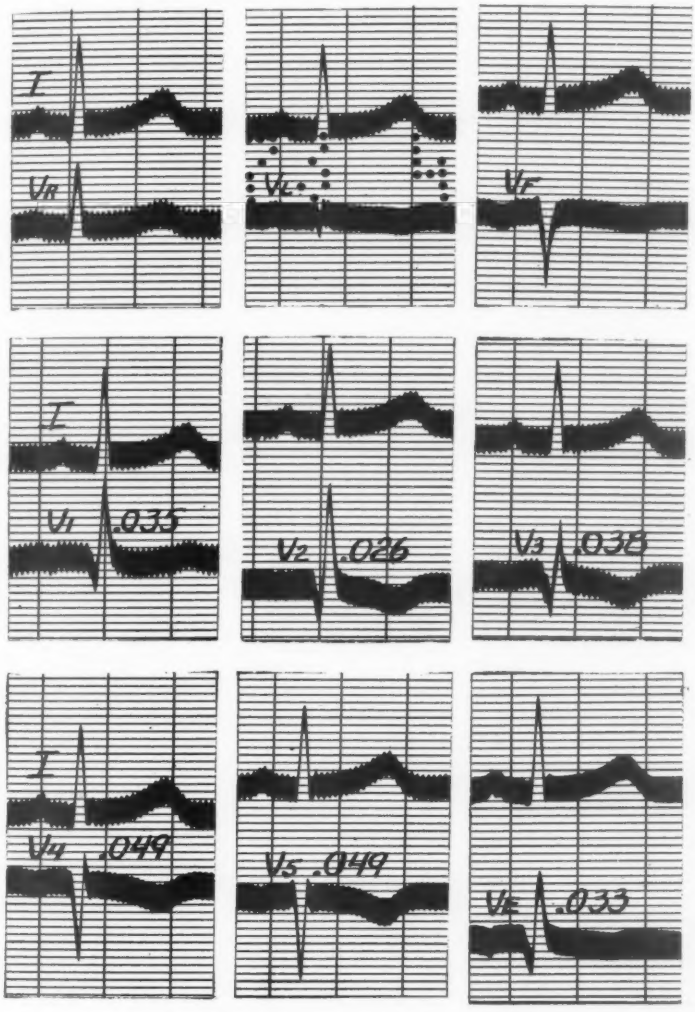

Fig. 4.—Extremity and precordial potentials of the subject whose standard electrocardiogram is shown in Fig. 3. In each instance the upper curve is standard Lead I. The lower curves represent the potential variations of the following points: V_R, right arm; V_L, left arm; V_F, left leg; V_1, fourth rib at right sternal edge; V_2, fourth rib at left sternal edge; V_3, fifth rib halfway between left sternal edge and left nipple line; V_4, fifth interspace just inside nipple line (apex); V_5, sixth rib anterior axillary line; V_E, ensiform cartilage. In the first three records 1 cm. equals 1 millivolt; in the last six 0.5 cm. equals 1 millivolt. The figures written on the records give the position of the chief upstroke of QRS with reference to the beginning of the QRS interval.

followed by a large upward movement. The chief upstroke occurs early in the QRS interval. The curves obtained from the left side of the precordium (V_4 and V_5) show a much deeper downward movement, and the chief upstroke is late. In one of these curves (V_5) a slight rise precedes the first descent. This summit is seldom if ever large in normal subjects. The potential variations of the right arm are similar to those recorded on the right side of the precordium, and the potential variations of the left leg are similar to those recorded on the left side of the precordium. As is usually the case in normal subjects, the potential variations of the left arm are small. In left axis deviation the chief deflection of the left arm lead is downward; in right axis deviation it is upward. The direction and size of this deflection may be used as a rough index in estimating the kind and grade of ventricular preponderance. Examination of equation (14) shows that it is similar in significance to the indices used for this purpose by Lewis[4] and by White and Boek.[5]

COMMENTS

It should be emphasized that the potential variations of the central terminal cannot be shown to be negligible unless certain assumptions are made. The assumptions referred to are those upon which Einthoven's method of determining the position of the electrical axis is based and especially the assumption that electromotive forces arising in the heart and having a direction perpendicular to the plane of the three standard leads have no effect upon the potential of the right arm, left arm, or left leg.* Some further discussion may serve to indicate the magnitude of the error that may have been introduced into our calculations by this last assumption.

Let us assume that the electrical field produced in the body at a given instant by the heart may be satisfactorily represented by the electrical field produced by a doublet located at the center of a homogeneous sphere of conducting material. At any point on the surface of such a sphere the potential due to a central doublet is proportional to the cosine of the angle between the radius drawn to that point and the axis of the doublet (Canfield,[6] Wilson, Macleod and Barker[7]). If the axis of the doublet is parallel to the plane determined by three surface points lying at the apices of an equilateral triangle, the mean potential of these points is zero. If the axis of the doublet is not parallel to the plane mentioned, the mean potential of the three points is not zero unless this plane passes through the center of the sphere. The doublet may be regarded as the sum of two components: a doublet whose axis is parallel and a doublet whose axis is perpendicular to the specified

*Einthoven's assumption that the heart is at the center of an equilateral triangle formed by the three leads amounts to the same thing, if it is understood to mean that the heart and the three leads are in the same plane. For his purpose, however, it was necessary to assume only that the heart is equidistant from the apices of this triangle.

plane. Any difference in potential between the three points must be attributed to the parallel component. The potential due to the perpendicular component is the same at all of them and is directly proportional to the distance from their plane to the center of the sphere. This is easily understood, for this distance measures the cosine of the angle formed by the radius drawn to any one of the three points and the axis of the perpendicular doublet.

The mean potential of four surface points lying at the apices of an equilateral tetrahedron is zero, whatever the position of the axis of the central doublet may be. The potential of a central terminal connected to four such points through like resistances must also be zero, and leads from this terminal to each of these points would give the data necessary for the determination of the orientation of the axis of the doublet in three-dimensional space. We have therefore considered the advisability of connecting the central terminal in our experiments not only to the right arm, left arm, and left leg, but also to an electrode placed on the back directly behind the heart. In the case of the theoretical model under consideration the error that would be made by considering the potential of the central terminal zero would be greater or less when it was connected to the apices of an equilateral triangle than when it was also connected to a fourth point at the more distant extremity of the diameter perpendicular to the plane of the triangle according as the distance from the plane of the triangle to the center of the sphere was more or less than one-seventh of the radius.* If the four points lay at the apices of an equilateral tetrahedron, this distance would, of course, be exactly one-third of the radius.

The plane of the three standard leads is not very well defined, but it would seem that it must be regarded as passing through the heart. If this is the case, it is improbable that connecting the central terminal to an additional electrode on the back would reduce whatever error is made by considering the potential of this terminal zero. This procedure may, however, prove useful for the purpose of determining the projection of the electrical axis upon a sagittal as well as upon a frontal plane. Over other ways of doing this it has the advantage that when the distances from the heart to the electrodes are unequal the error made by assuming that the heart is at the center and the electrodes are at the apices of an equilateral tetrahedron (or triangle) may be partly or wholly eliminated by making the resistances between the central terminal and the electrodes unequal.

*The error made by using the four points specified could be corrected by making the resistance between the fourth point and the central terminal greater or less than the other three. If, for example, the distance from the plane of the triangle to the center of the sphere was exactly one-seventh of the radius it would be necessary in order to bring the potential of the central terminal to zero to make this resistance seven-thirds of the resistance between the central terminal and each apex of the triangle.

SUMMARY

In order to simplify the analysis of the curves obtained by leading from the precordium and for certain other purposes, we have devised leads that record the potential variations of a single electrode.

Electrodes are placed on the right arm, left arm, and left leg in the usual way and connected through like resistances to a central terminal. The resistances used for this purpose should be large in comparison with the resistance of the body in standard leads. Theoretical considerations and experiments on a model indicate that under these circumstances the potential variations of the central terminal are negligible.

The curves obtained by leading from an exploring electrode in contact with any part of the body to the central terminal represent the variations in potential produced by the heartbeat in the region in contact with the former. The potential variations of the right arm, left arm, and left leg are recorded by leading from the electrodes placed on these extremities to the central terminal. They may be compared with the potential variations that occur in various parts of the precordium.

To increase the resistance in the input circuit of our recording apparatus we have connected the string galvanometer to the balanced plate circuit of a one-stage vacuum-tube amplifier.

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THE SIGNIFICANCE OF ELECTROCARDIOGRAMS CHARACTERIZED BY AN ABNORMALLY LONG QRS INTERVAL AND BY BROAD S-DEFLECTIONS IN LEAD I*

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INTRODUCTION

IN A previous publication[1] it was shown that the order in which the two ventricles pass into the excited state in human bundle-branch block can be determined by means of serial precordial leads. It was pointed out that such leads might be expected to prove useful in the study of the electrocardiographic changes produced by ventricular hypertrophy by coronary occlusion, and by intraventricular block. Further experience has tended to confirm this opinion. A number of cases of coronary occlusion have been studied, and the peculiarities of the precordial electrocardiogram in this condition have been briefly described.[2] In an experimental study of myocardial infarction recently completed it was found that the ventricular complexes of precordial, of semidirect, and of direct leads are altered in the same way. Meanwhile we have collected considerable material bearing upon the significance of various types of electrocardiograms which indicate the presence of high grade intraventricular block, but do not display all the characteristics generally considered necessary for the diagnosis of bundle-branch block. It is our present purpose to consider a group of curves that show a QRS interval measuring 0.12 second or more, a broad S-deflection in Lead I, and certain other features described on the following pages.

We have made some changes in the method of taking precordial leads described previously.[1] When we first began to make use of such leads, we placed one electrode (the exploring electrode) upon the precordium and the other (the indifferent electrode) upon the left leg. The chief features of the curves so taken are determined by the potential variations of the exploring electrode. These are usually very large in comparison with the potential variations of the indifferent electrode, but the latter cannot always be regarded as negligible. In order to reduce or eliminate them, and thus make precordial curves more nearly com-

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parable to those obtained by direct and semi-direct leads in animals, we have adopted the following procedure. The indifferent electrode is replaced by a central terminal joined to electrodes on the right arm, left arm, and left leg by like resistances of 5,000 ohms or more. The central terminal and the exploring electrode are connected to the input terminals of a vacuum tube with a balanced plate circuit in which the string galvanometer is inserted. The principles upon which this method of leading is based are fully discussed in the preceding article. As is there shown, it yields curves which represent the potential variations of any part of the body in contact with the exploring electrode. This method has been used in obtaining the majority of the curves described and reproduced in this article. The curves that represent the potential variations of precordial points are designated by the symbols V_1, V_2, etc.; those that represent the potential variations of the right arm, left arm, and left leg are labelled V_R, V_L, and V_F, respectively. In taking the former the string galvanometer is ordinarily used at half the normal sensitivity; in taking the latter it is used at the normal sensitivity. In all these special leads the connections are so arranged that a negative variation in the potential of the exploring electrode is represented by an upward, a positive variation by a downward movement of the string shadow.

DESCRIPTION OF CLINICAL CURVES

The patient whose electrocardiograms are shown in Fig. 1 was a man, aged seventy-one years, who was under treatment in the surgical division of the hospital for carcinoma of the prostate gland with retention of urine. He had no complaints that could be referred to the heart. The systolic blood pressure was 185 mm. Hg; the diastolic pressure 90 mm. Hg. The electrocardiogram was taken at the suggestion of a consultant who found slight enlargement of the heart and a few râles at the lung bases.

Most cardiologists would probably consider the standard electrocardiograms (Fig. 1) as sufficiently characteristic to warrant a diagnosis of bundle-branch block of the rare type. The QRS interval measures approximately 0.158 second. In Lead I the R-deflection and the S-deflection are nearly equal in size, but the former is narrow while the latter is very broad. In Lead III there is an unusually prominent Q-deflection followed by a tall R, which is notched and stands upon an exceptionally wide base. The ventricular complexes in Lead II are similar to those in Lead III. The T-deflections are upright in Lead I and inverted in Leads II and III, but are relatively small in all leads.

Curves were taken from six precordial points. In the first of these (V_1), which was taken from the point farthest to the right, and in the last (V_E), which was taken by placing the exploring electrode over

the ensiform cartilage, the chief upstroke of QRS is very late. It occurs approximately 0.1 second after the first deflection in Lead I. In the curves taken from the left side of the precordium (V_3, V_4, and V_5), on the other hand, the chief upstroke of QRS is relatively early. It begins about 0.04 second after the first deflection in Lead I and is nearly synchronous with the peak of R in this lead. The second precordial curve (V_2) may be regarded as transitional between those taken farther to the right and those taken farther to the left; it shows both an early and a late upstroke.

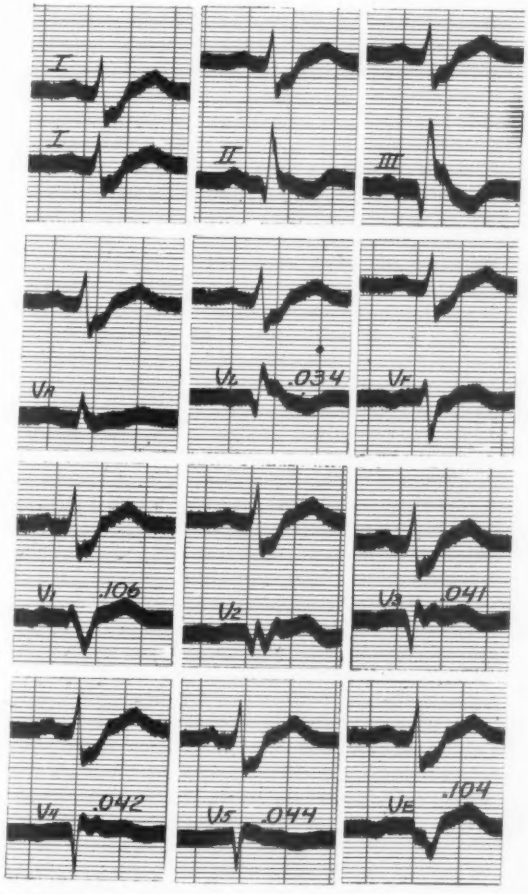

Fig. 1.—QRS interval, 0.158 second. All the figures reproduced in this article show standard Lead I (above) and a second curve (below) taken simultaneously with it. The explanatory notes of the legends refer to the lower curve only. I, Standard Lead I; II, standard Lead II; III, standard Lead III. V_R, potential variations of the right arm; V_L, potential variations of the left arm; V_F, potential variations of the left leg. The last six curves represent the potential variations of the following precordial points; V_1, fourth costal cartilage, right sternal edge; V_2, fourth interspace, left sternal edge; V_3, fifth rib, halfway between the left sternal edge and the nipple line; V_4, fifth interspace, left nipple line; V_5, sixth rib, left anterior axillary line; V_6, ensiform cartilage. A curve not reproduced from the sixth interspace in the midaxillary line is very similar to V_5. The first six curves were taken with the string galvanometer at the normal sensitivity (1 cm. squals 1 millivolt); the last six records were taken with the galvanometer at one-half the normal sensitivity (1 cm. equals 2 millivolts). The interval in seconds from the beginning of the QRS interval to the onset of the chief upstroke of QRS, when this is well defined, is written on the records.

In this particular instance the curves that represent the potential variations of the extremities (V_R, V_L, and V_F) do not, as is often the case, closely resemble the precordial curves. The left arm curve (V_L) is somewhat like those obtained from the left side of the precordium; the main upstroke is early, and the final portions of QRS lie above the base line. The left leg curve (V_F) is more like the first precordial curve than any of the others, but its chief upstroke is earlier. The right arm curve (V_R) is small.

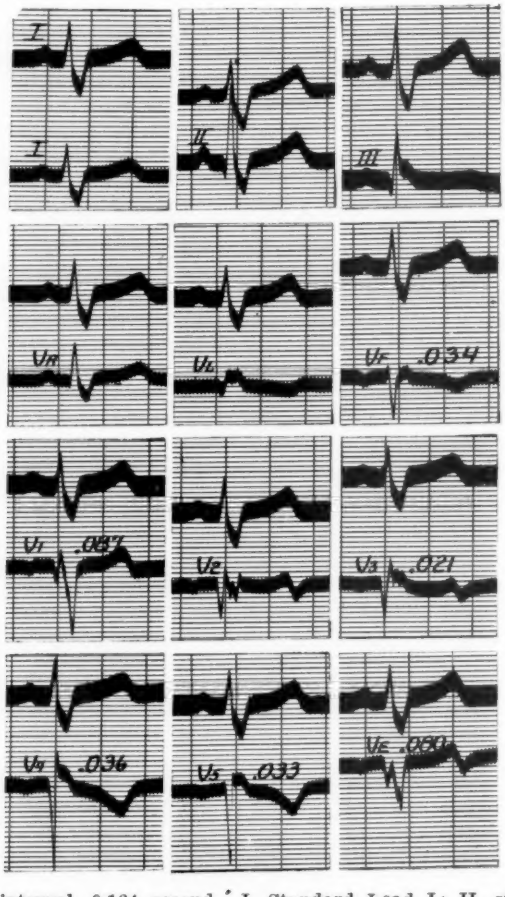

Fig. 2.—QRS interval, 0.124 second. I, Standard Lead I; II, standard Lead II, III, standard Lead III. V_R, Potential variations of the right arm; V_L, potential variations of the left arm; V_F, potential variations of the left leg. The last six curves represent potential variations of the following precordial points: V_1, fourth costal cartilage, right sternal edge; V_2, fourth interspace, left sternal edge; V_3, fifth rib, halfway between left sternal edge and left nipple line; V_4, fifth interspace, left nipple line (apex); V_5, sixth rib, anterior axillary line; V_6, ensiform cartilage. A curve (not reproduced) from the sixth interspace in the midaxillary line is very similar to V_5. The first six curves were taken with the galvanometer at the normal sensitivity; the last six with the galvanometer at half the normal sensitivity.

A second set of electrocardiograms of the same type is shown in Fig. 2. The patient was a boy, aged eleven years, who was being treated for left-sided pleural effusion and acute gonorrheal urethritis.

The physical examination of the heart showed no enlargement, no valve lesions, and no other signs that could be considered abnormal. The blood pressure was normal, and there was no evidence of nephritis or of anemia. The Kahn test was negative. There was no history of rheumatic fever or other infections that might have damaged the heart, and the cause of the intraventricular block was obscure. After a month in the hospital the patient was discharged apparently quite well; the electrocardiogram had not changed.

In general outline the ventricular complexes of the standard leads (Fig. 2) are similar to those of Fig. 1. The QRS interval measures

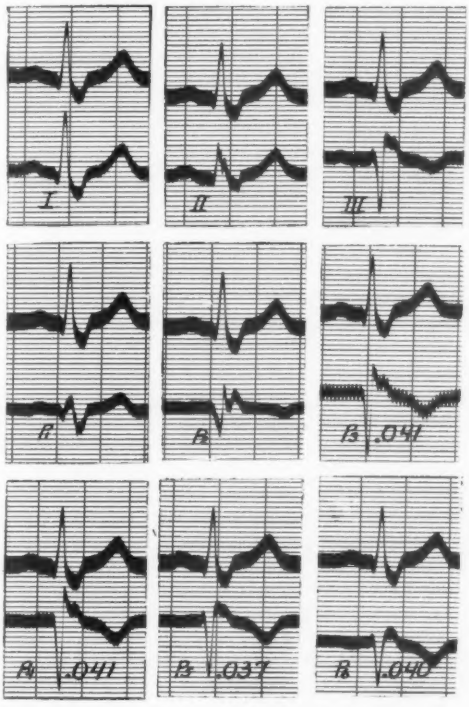

Fig. 3.—QRS interval, 0.138 second. I, Standard Lead I; II, standard Lead II; III, standard Lead III. The last six curves are precordial electrocardiograms taken by placing the indifferent electrode on the left leg and the exploring electrode on the following precordial points: P_1, third interspace, right sternal edge; P_2, third interspace, left sternal edge; P_3, third interspace, midclavicular line; P_4, fifth interspace, 3 cm. to the left of the midclavicular line (apex); P_5, fifth interspace, anterior axillary line; P_6, sixth interspace, midaxillary line. The first three curves were taken with the galvanometer at the normal sensitivity; the last six with the galvanometer at half the normal sensitivity.

approximately 0.124 second. The R spike is prominent in all three leads particularly in Lead II. In Leads I and II it is narrow, but in Lead III it is wide and notched. There is a broad S-deflection in Leads I and II, and a prominent Q in Leads II and III. The resemblance between the precordial curves and the corresponding curves of Fig. 1 is striking. The chief upstroke of QRS in the first of these curves (V_1) occurs near the end of the QRS interval, approximately

0.087 second after the first deflection in Lead I. The chief upstroke of the ensiform curve (V_E) is nearly as late. In the curves taken from the left side of the precordium (V_3, V_4, and V_5) the chief upstroke is almost synchronous with the peak of R in Lead I; in the different curves it begins 0.021 to 0.036 second after the first deflection in Lead I. The second precordial curve (V_2) is of the transitional variety.

The left leg curve is similar to those taken from the left side of the precordium, and the chief upstroke occurs at about the same time. The left leg may therefore be regarded as lying in the left ventricular field. The right arm curve is like the curves from the right side of the precordium, but the resemblance is not close. The left arm curve is small.

The patient whose electrocardiograms are shown in Fig. 3 was a woman, aged sixty-four years, who was under treatment in the hospital for chronic atrophic arthritis, inguinal hernia and anal fistula. She had no complaints referable to the heart, and the physical examination of the heart showed nothing abnormal except slight enlargement and accentuation of the aortic second sound. The blood pressure was normal; the Kahn test was negative.

The standard electrocardiograms (Fig. 3) differ from those of the other two patients in several respects. In Lead I the narrow R spike is much more prominent than the broad S-wave and is preceded by a small Q-deflection. In Lead III the deep downstroke is preceded by a small upward movement; a broad upward movement occurs synchronously with S in Lead I. Curves of this type are common. They have not ordinarily been attributed to right branch block. In this case the precordial leads were taken by the old method of placing the indifferent electrode on the left leg. Nevertheless they are similar in every way to the corresponding curves of Figs. 1 and 2. Here again the chief upstroke of QRS is late in the first precordial lead and early in the curves taken from the left side of the precordium. In the latter it is practically synchronous with the peak of R in Lead I and occurs about 0.04 second after the first deflection in this lead. The second precordial curve is again of the transitional type.

AN ANIMAL EXPERIMENT

The three sets of precordial curves described are strikingly similar. They are of the type that is obtained in right branch block in the dog. In order to demonstrate the resemblance between these clinical curves and experimental curves taken in the same way we may describe an experiment performed on this animal.

A large dog was fully anesthetized with morphine and ether, and the heart was exposed under aseptic precautions by the following

method. A large flap of skin and muscle in the precordium was turned back, the pleural cavity was opened by cutting through one of the interspaces, and the adjoining ribs were retracted. While respiration was maintained artificially, a small slit was made in the pericardium just below the origin of the pulmonary artery, and the right branch of the His bundle was cut by thrusting a small knife through the wall of the conus arteriosus and pressing it against the interventricular septum in the usual way. The pericardium and the chest were then carefully closed, and the animal was allowed to recover. Eight days later the dog was anesthetized with morphine and urethane and brought to the electrocardiographic laboratory. After the three standard leads had been taken, three copper disks with binding posts attached were sewn beneath the skin of the chest. These disks were arranged along a line passing across the precordium in a base-apex direction and mak-

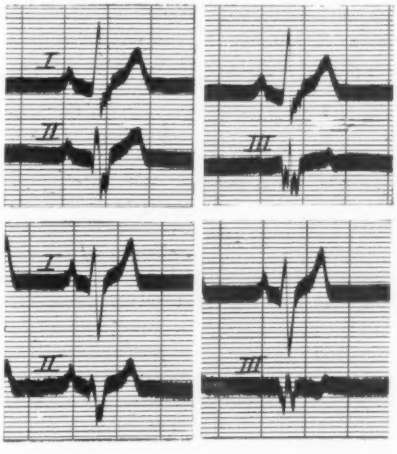

Fig. 4.—Standard electrocardiograms of a dog with bundle-branch block produced by section of the His bundle eight days before. The curves in the upper row were taken before, and those in the lower row after opening the chest. The QRS interval is approximately 0.093 second. Opening the chest altered the form of the ventricular complex, particularly in Lead I. In this lead the interval from the beginning of the QRS interval to the peak of R measures approximately 0.028 second.

ing an angle of sixty-five degrees with the midsternal line, which it crossed 19 cm. from the episternal notch. The first disk was placed 9 cm. to the right of the midline, the second in the midline, and the third 9 cm. to the left of the midline. Using these disks as exploring electrodes two sets of leads were taken. In the first set the indifferent electrode was placed on the left leg; in the second a central terminal connected to the two fore legs, and the left hind leg through resistances of 5,000 ohms was substituted for the indifferent electrode. The two sets of curves are similar but show minor differences (Fig. 4). After splitting the sternum the pericardium was cut along a line parallel to the long axis of the heart, and the cut edges were sewn to the margins of the chest wound. The exposed heart was now cov-

ered with a pad of gauze soaked in normal saline solution, and a set of pad leads was taken. The method employed was the same as in the study of bundle-branch block[1] previously referred to except that the central terminal, instead of the left hind leg, was used as the indifferent point. The pad of gauze was then removed and a series of direct leads from the anterior surface of the heart to the central terminal, and a second set of standard leads were taken. At the end of the experiment the animal was killed, and the heart was removed and opened. A rather superficial cut crossing the course of the right

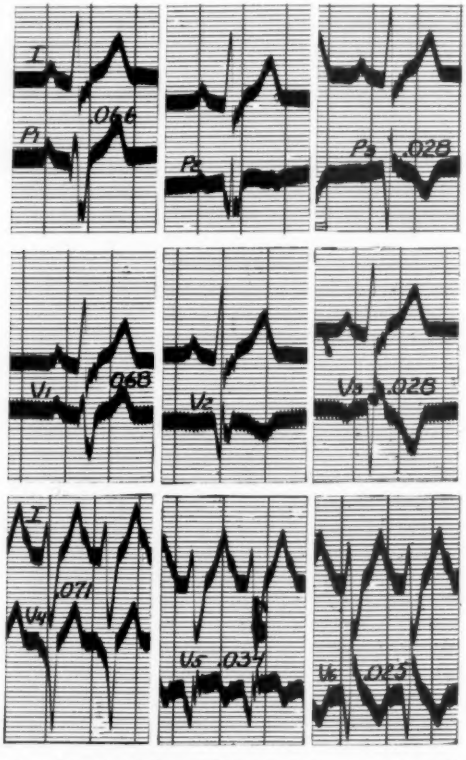

Fig. 5.—Precordial and pad electrocardiograms in experimental right branch block. In taking the first three records the indifferent electrode was placed on the left hind leg; in taking the last six a central terminal connected to the three extremities through resistances of 5,000 ohms (see text) was substituted for the indifferent electrode. In taking the curves of the second row the same exploring electrodes were used as in taking the corresponding curves of the first row. The exploring electrode for P_1 and V_1, was 9 cm. to the right of the midline; the exploring electrode for P_2 and V_2 was in the midline; and the exploring electrode for P_3 and V_3 was 9 cm. to the left of the midline. The last three curves were taken with the exploring electrode in contact with a gauze pad soaked in normal saline solution and laid upon the exposed heart. This electrode was placed upon the right basal portion of the pad for V_4, on the central portion for V_5, and on the left apical portion for V_6. The first six records were taken with the galvanometer at the normal sensitivity; the last three with the galvanometer at three-twentieths of the normal sensitivity.

branch of the His bundle in its basal half and covered by a small amount of adherent thrombus was found.

The Experimental Curves.—The form of the ventricular complex in standard leads was considerably altered by opening the chest. In the

curves taken before opening the chest the ventricular complexes of Lead I are strikingly similar to the ventricular complexes of the same lead in the clinical curves we have described; R is tall and narrow, S is shallow and broad, and T is upright. In the curves taken after opening the chest the ventricular complexes of Lead I are quite different (R is much shorter and S much deeper) and resemble in general outline those usually obtained after section of the right bundle-branch. Both the curves taken before and those taken after opening the chest show much larger ventricular deflections in Lead I and much smaller ventricular deflections in Lead III than are ordinarily obtained after right branch section. Practically all the canine right branch block curves described or reproduced in the literature were taken with the chest open. Lewis[3] states that restoration of the chest in his experi-

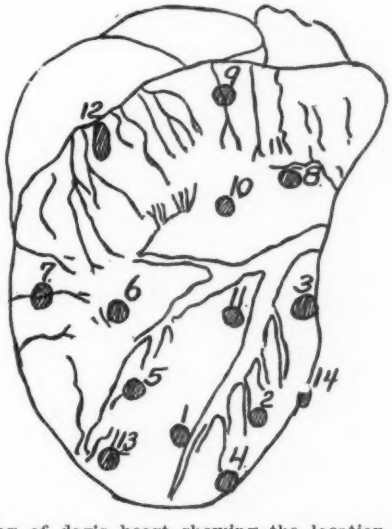

Fig. 6.—Outline drawing of dog's heart showing the location of the exploring electrode in taking the direct curves shown in Fig. 7.

ments did not alter the form of the ventricular complex materially. At the present time, however, we do not know definitely how large a part exposing the heart plays in determining the form of these curves as we know them.

The resemblance between the human and the canine precordial curves (Fig. 5) is striking. In the first precordial lead the chief upstroke is late; it occurs about 0.068 second after the first deflection in Lead I. The last precordial lead, on the other hand, shows an early upstroke practically synchronous with the peak of R; it begins about 0.028 second after the first deflection in Lead I. The ventricular complexes of the second precordial lead are of the transitional type. The pad curves are similar to the precordial curves. The chief upstroke is late in the first, which was taken from that part of the pad which lay upon

the right ventricle, and early in the last, which was taken from that part of the pad that lay on the left ventricle. In the second pad curve the chief upstroke is early, but in relative size and in shape the ventricular complexes are like those referred to as transitional.

Most of the direct curves are reproduced in Fig. 7, and the location of the points from which they were taken is shown on an outline drawing of the heart in Fig. 6. The curves taken from points on the basal portion of the right ventricle show a very late chief upstroke or in-

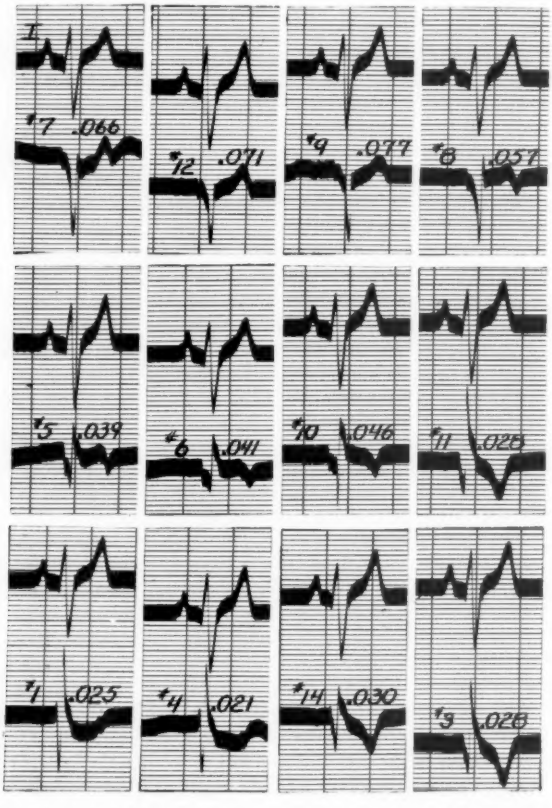

Fig. 7.—Direct electrocardiograms from the points indicated in Fig. 6. In taking these curves a central terminal connected to the three extremities (see text) was used as the indifferent point, and the galvanometer was used at one-twentieth normal sensitivity. The figures written on the records show the interval in seconds from the onset of the first deflection of the QRS group in Lead I to the chief upstroke of the direct curves. The curve (not reproduced) from point 2 is very similar to those from points 1 and 4; the curve from point 13 is very similar to those from points 5 and 6. In all figures of this article the intervals between the time lines are fifths of a second.

trinsic deflection, which begins 0.057 to 0.077 second after the first deflection in Lead I. The ventricular complexes resemble the first pad curve and that obtained from the right side of the precordium in general outline, but lack the well-defined upward movement that precedes the main downstroke in the latter.

The curves taken from the apical portions of the left ventricle closely resemble the last pad curve and that obtained from the left side of the precordium. The chief upstroke occurs 0.021 to 0.030 second after the first deflection in Lead I and is nearly synchronous with the peak of R in this lead. The direct curves show the same broad upward movement synchronous with S in Lead I that is seen in the last pad and in the last precordial curve. In these curves, however, the small upstroke that precedes the main downward movement in most of the direct curves is absent.

The direct curves from points near the attachment of the interventricular septum are somewhat variable in form. In a general way they correspond in type to the pad and precordial curves that we have classed as transitional. The chief upstroke occurs about 0.04 second after the first deflection in Lead I; the ventricular deflections are of small amplitude. These curves, however, show only one upstroke.

DISCUSSION

The striking resemblance between the direct, the pad and the precordial curves in this experiment strongly supports the view that the ventricular complex in precordial leads in man is similar in general outline and as regards the position of the chief upstroke in the QRS interval to the curves that would be obtained by leading directly from the epicardial surface of the subjacent portions of the heart wall. When there is a conduction defect that greatly delays the activation of the anterior surface of one ventricle without affecting the time of activation of the anterior surface of the other, the curves from the two sides of the precordium are, as a rule, so unlike that there is little chance of locating the conduction defect on the wrong side. There are, however, one or two features of the precordial curves obtained in branch block that are rather puzzling. In the rare type of branch block the transition from complexes showing a late chief upstroke to complexes showing an early chief upstroke generally occurs considerably farther to the right than the transition from complexes of the last to complexes of the first kind in branch block of the common variety. The principal reason seems to be that in branch block the delay in the arrival of the excitation wave at the epicardial surface is much less for those portions of the homolateral ventricle that lie near the septum than for those that are at a greater distance from it. A second peculiarity of the precordial curves in right branch block is the prominent upstroke at the beginning of QRS in the leads taken furthest to the right. This deflection occurs in canine as well as in human curves. No similar deflection is present in direct curves from the right ventricle of dogs with right branch block. For the time being the origin of this summit remains obscure.

Clinical curves of the kind described in this article are evidently due to a conduction defect that delays the activation of the anterior surface of the right ventricle; in all probability to complete right bundle-branch block. This conclusion is based upon the resemblance between the human precordial curves and those obtained in canine right branch block, and upon the resemblance between the ventricular complexes in Lead I taken before opening the chest in the experiment we have described and the ventricular complexes of the clinical curves in the same lead.

Until quite recently human branch block curves of the common type were almost universally accepted as evidence of a defect in conduction in the right branch of the His bundle. Such curves are discordant and are usually truly diphasic. In Lead I the broad initial deflection is upward and the large T-wave is inverted; in Lead III the broad initial deflection is downward and T is upright. In Lead I there may be a small Q; more often it is absent. In Lead III there is frequently a small R, but it is seldom if ever large. It was supposed that left branch block must be represented by diphasic curves of the opposite kind. Such curves proved to be exceedingly rare in comparison with those just described, and this was attributed to the difference in character between the right and left branches of the His bundle. The former is long and slender and gives off no early branches; it receives its blood supply from a single source. The latter is short and broad and branches almost at once; the more dorsal and the more ventral of its major subdivisions have a different blood supply. It seemed proper, therefore, that the right branch of the bundle should be the more vulnerable and that right branch block should be twenty or more times as common as left. It may be pointed out, however, that our ideas regarding the frequency of the two varieties of branch block depend to a very large extent upon the criteria that we set up for the diagnosis of lesions on the one side and on the other. It is probable that both right and left branch block are considerably more common than is at present believed.

In the dog the curves that represent right branch block differ from those that represent left branch block in respect to the direction of the broad initial deflection and of the T-wave in standard leads, but the two kinds of curves are not, strictly speaking, opposites. As a rule, the latter are truly diphasic, but the former are often far from it. They almost always show a very conspicuous R-deflection preceding the broad S, and the first deflection is often one-third to one-half as large, though not as broad, as the second. It may even be larger in some leads as in the instance described in this paper.* One might expect that a similar deflection would frequently be seen in human right branch block, and we believe that this is frequently the case.

*We have already pointed out that practically all canine branch block curves described in the literature were taken with the chest open. We do not know whether R in Lead I will prove to be uniformly larger when the chest is intact.

The prominent R-deflection in canine right branch block seems to be due to electric forces produced by activation of certain portions of the free wall of the left ventricle. A similar deflection in the opposite direction is absent in left branch block, probably because the free wall of the right ventricle is much thinner than that of the left. In support of this surmise regarding the origin of R in experimental right branch block we call attention to the very deep downstroke that occurs in direct leads from the apical portions of the anterior surface of the left ventricle, and in leads from the left side of the precordium. This downstroke is synchronous with R in Lead I, and it seems probable that the two deflections have a similar origin. The question arises, therefore, whether the R-deflection in Lead I and the corresponding Q or S deflection in Lead III in human right branch block do not tend to be larger when the left ventricular wall is thicker. It may be that left ventricular hypertrophy tends to modify right branch block curves in this manner.

In conclusion we believe that the clinical curves described in this article represent right bundle-branch block, and have the same significance as the discordant diphasic complexes long regarded as characteristic of branch block of the rare type.

SUMMARY

Serial precordial leads have been used in an attempt to locate the conduction defect responsible for electrocardiograms characterized by a QRS interval measuring 0.12 second or more and by narrow R-deflections and broad S-deflections in Lead I. In Lead III there is a narrow Q or S deflection synchronous with R in Lead I and a broad upward deflection synchronous with S in the same lead.

In cases in which the standard electrocardiogram is of this type precordial leads from the right side of the precordium show a very late chief upstroke; precordial leads from the left side of the precordium show an early chief upstroke approximately synchronous with the peak of R in Lead I. These curves are strikingly similar to those obtained by the same method of leading after section of the right branch of the His bundle in dogs.

For this reason it is believed that electrocardiograms of the kind mentioned represent right bundle-branch block in man. There is much less difference in frequency between clinical right and clinical left branch block than has heretofore been supposed.

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ELECTROCARDIOGRAMS OF AN UNUSUAL TYPE IN RIGHT BUNDLE-BRANCH BLOCK*

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IN PREVIOUS articles[1, 2] it has been shown that precordial leads are of great value in locating intraventricular conduction defects. The form of the ventricular deflections in such leads indicates that in man right bundle-branch block is often represented by ventricular complexes characterized by a broad S-deflection in Lead I, a simultaneous broad upward deflection in Lead III, and an abnormally long QRS interval. In this article we present evidence that it is occasionally represented by ventricular complexes of a different kind. In Lead III complexes of the type to which we refer are similar to those seen in left branch block, but in Lead I all the ventricular deflections are of low voltage and the last deflection of the QRS group is downward. Precordial leads have been employed in three cases in which the standard electrocardiogram was of this class.

CASE 1.—The first patient was a man, thirty-seven years old, who had suffered from severe bronchial asthma for the last three or four years. The symptoms were those characteristic of this condition, and the attacks were relieved by adrenalin. For the preceding month dyspnea had been almost continuous. Examination of the lungs showed emphysema, wheezing expiration, and many sibilant râles. The heart was moderately enlarged; an orthodiagram showed a frontal plane area 48 per cent larger than that found in normal subjects of similar size. The blood pressure was not increased, and no valve lesions could be detected. There was a history of chancre twelve years before, but the Kahn test was negative. Examination of the blood showed nothing abnormal. Treatment with adrenalin, ephedrine, and vaccines, and the elimination of foods that gave positive skin tests were followed by slight improvement, but frequent asthmatic attacks continued. About two months after the patient first came to the hospital, the heart rate, which had always been within normal limits, suddenly rose to approximately 180 per minute. At the same time the rhythm became conspicuously irregular. The abnormal rhythm lasted about four hours and ended, as suddenly as it began, one-half to one hour after the administration of a second 0.2 gram dose of quinidine sulphate by mouth. The first electrocardiogram was taken shortly after the onset of this attack. It shows strikingly abnormal, diphasic ventricular complexes of the discordant type. The chief deflection of the QRS group is downward in Lead I and upward in Leads II and III; there is a pronounced alternation in the amplitude of all the ventricular deflections. The ventricular rhythm is decidedly irregular. No auricular deflections can be clearly discerned. It was thought that the paroxysm was of ventricular

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origin. An electrocardiogram taken on the following day shows normal sinus rhythm interrupted by frequent ventricular extrasystoles, which are represented by complexes similar to those recorded during the attack. In this electrocardiogram and in those taken subsequently the ventricular responses to the auricle are represented by complexes of the kind shown in Fig. 1.

In Lead I all the ventricular deflections are small. The last deflection of the QRS group is the largest and it is downward. In Leads II and III there is a small R followed by a deep broad S, and T is upright. The QRS interval is approximately 0.167 second. At first we were under the impression that these curves were an

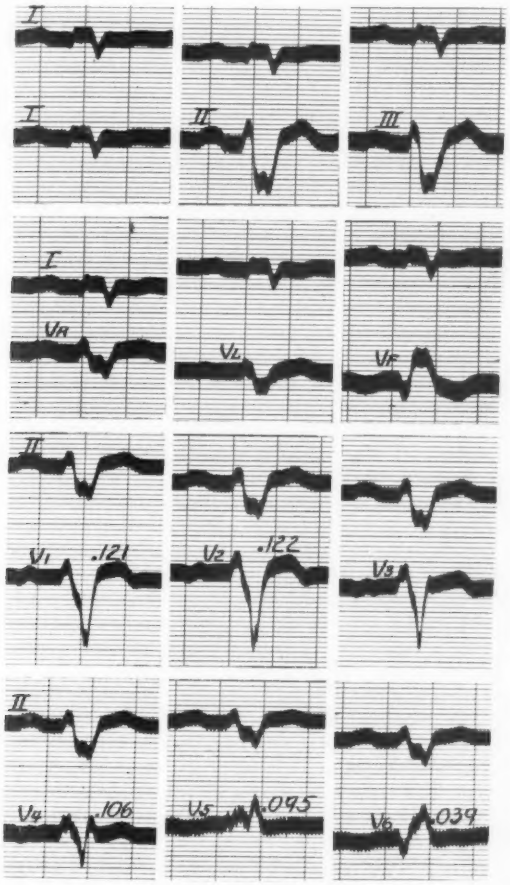

Fig. 1.—Case 1. QRS interval, 0.167 second. The upper curve of the first six records is standard Lead I; the upper curve of the last six records is standard Lead II reduced to about one-half its normal amplitude. The notes that follow refer to the lower curve of each record: I, standard Lead I; II, standard Lead II; III, standard Lead III; V_R, potential variations of the right arm; V_L, potential variations of the left arm; V_F, potential variations of the left leg. The last six curves represent the potential variations of the following precordial points: V_1, fourth costal cartilage at right edge of sternum; V_2, fourth interspace at left edge of sternum; V_3, fifth rib halfway between left sternal edge and left nipple line; V_4, fifth interspace in left nipple line; V_5, sixth rib left anterior axillary line; V_6, sixth rib left midaxillary line. The precordial curves were taken with the galvanometer at seven-tenths of the normal sensitivity (7 mm. equal 1 millivolt). The remaining curves were taken with the galvanometer at normal sensitivity. The figures written on the records give the interval from the first deflection of the QRS group in Lead II to the beginning of the chief upstroke of QRS in the lower curve. In all the records reproduced in this article the time lines indicate fifths of a second.

unusual variant of the kind seen in bundle-branch block of the common variety (left branch block), but when precordial electrocardiograms were taken, it was obvious that this was not the case.*

In the leads from the right side of the precordium (V_1, V_2, and V_3) the chief upstroke of QRS is very late. It occurs near the end of the QRS interval and begins about 0.12 second after the earliest ventricular deflection in Lead II. In the leads from the left side (V_5 and V_6) of the precordium the chief upstroke of QRS is somewhat earlier, but is poorly defined. The precordial electrocardiograms are similar to

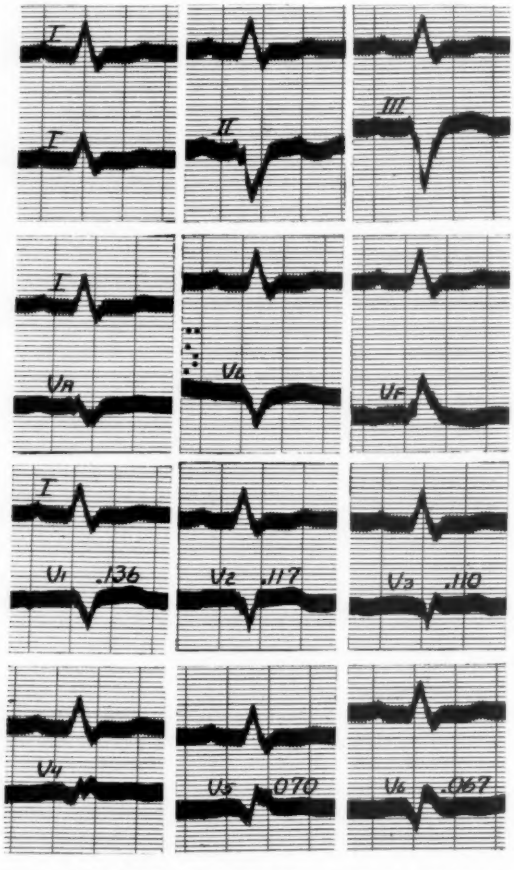

Fig. 2.—Case 2. QRS interval, 0.177 second. In each record the upper curve is standard Lead I. The notes that follow refer to the lower curves only. I, standard Lead I; II, standard Lead II; III, standard Lead III; V_R, potential variations of the right arm; V_L, potential variations of left arm; V_F, potential variations of the left leg. The last six curves represent the potential variations of the following precordial points: V_1, fourth rib right sternal edge; V_2, fourth interspace left sternal edge; V_3, fifth rib halfway between the left sternal edge and the left nipple line; V_4, fifth interspace left nipple line; V_5, sixth rib left anterior axillary line; V_6, sixth rib left midaxillary line. The figures written on the records give the interval in seconds between the first deflection of the QRS group in Lead I and the beginning of the chief upstroke of QRS in the lower curve. The precordial curves were taken with the galvanometer at half the normal sensitivity; the remaining curves were taken with the galvanometer at the normal sensitivity.

*In taking these precordial curves and all others described in this article, a central terminal connected to the right arm, left arm, and left leg through resistances of 5,000 ohms was used as the indifferent point. This method has been described elsewhere;[3] it yields curves that may be regarded as representing the potential variations of the exploring electrode.

those that have been shown[1, 2] to be characteristic of right branch block in the dog and of branch block of the rare type in man. The chief differences are that in the present case the area over which complexes with a late chief upstroke were recorded extended somewhat further to the left than is usual, and that in the leads from the left side of the precordium the chief upstroke of QRS rises slowly and is of small amplitude. The curves that represent the potential variations of the right arm and left arm are like those obtained from the right side of the precordium; the curve that represents the potential variations of the left leg is like those obtained from the left side of the precordium.

CASE 2.—The second patient was a man, forty-eight years old, who came to the hospital complaining of attacks of unconsciousness. These attacks were of short duration and came on without warning. They were accompanied by a gripping sensation in the epigastrium, and a feeling of pressure under the sternum. The first attack had occurred four months before, and he had had several since. There was no enlargement of the heart; an orthodiagram showed a frontal plane area within normal limits. The systolic blood pressure was 125 mm. Hg; the diastolic 85 mm. Hg. The heart rate was 75 per minute and no murmurs could be detected. The heart sounds were very distant. The Kahn test and the examination of the urine were negative.

The electrocardiograms are shown in Fig. 2. The standard curves, the precordial curves, and those that represent the potential variations of the extremities are strikingly similar to the corresponding curves of Fig. 1. The QRS interval measures approximately 0.177 second. In Lead I the ventricular deflections are small. The chief deflection of the QRS group is upward, but there is a prominent deflection downward at the end of the QRS interval. In Leads II and III there is a small R followed by a deep broad S. In the leads from the right side of the precordium the chief upstroke of QRS is late; it occurs about 0.11 second after the beginning of the QRS interval. In the leads from the left side of the precordium, on the other hand, the chief upstroke of QRS occurs somewhat earlier. In these leads it begins about 0.07 second after the beginning of the QRS interval, and is somewhat better defined than in the corresponding curves of Fig. 1. The potential variations of the right and left arms indicate that these two extremities lay in the right ventricular field; the left leg was in the left ventricular field.

CASE 3.—The third patient was a farmer, aged fifty-eight years, who came to the hospital because of an inguinal hernia and shortness of breath on exertion. The latter had been noticeable for about three months, but had been worse for the past month. On one occasion some ten days before he had had to sit up all night because of nausea, vomiting, and breathlessness. Since that time there had been some pain in the precordium, but apparently it had not been severe. Ten days before coming to the hospital the patient had observed a painful red spot about two inches in diameter on the medial aspect of the lower left leg, and three or four days later the whole leg became tender. It was still red and somewhat swollen.

On examination the heart appeared to be slightly enlarged. There were no murmurs or other adventitious sounds. The heart sounds were distant. The heart rate was 80 per minute, and the rhythm was regular. The systolic blood pressure was 150 mm. Hg; the diastolic 90 mm. Hg. A few moist râles were heard at the lung bases. The condition of the left leg, which was swollen and tender, was thought to be due to venous thrombosis and thrombophlebitis. The Kahn test was negative. About three days after entering the hospital the patient suddenly began to complain of severe precordial pain, which was accompanied by profuse sweating, pallor, cyanosis, vomiting, and obvious dyspnea. It was not relieved by nitro-

glycerin, and morphine was given. On the following day there was some precordial pain and pronounced shortness of breath. The systolic blood pressure had fallen to 100 mm. Hg, and there was slight fever and a definite leucocytosis (16,000 white cells per c. mm.). After this the patient's condition was poor; he continued to complain of shortness of breath, precordial pain and vomiting. The pulse became very rapid and irregular and Cheyne-Stokes respiration frequently occurred. About one week after the attack described he had a severe chill, followed by high fever. He became moribund and died on the following night. An electrocardiogram taken soon after the patient was admitted to the hospital shows normal sinus rhythm. A second taken on the day of the attack shows sinus tachycardia (rate about 140 per

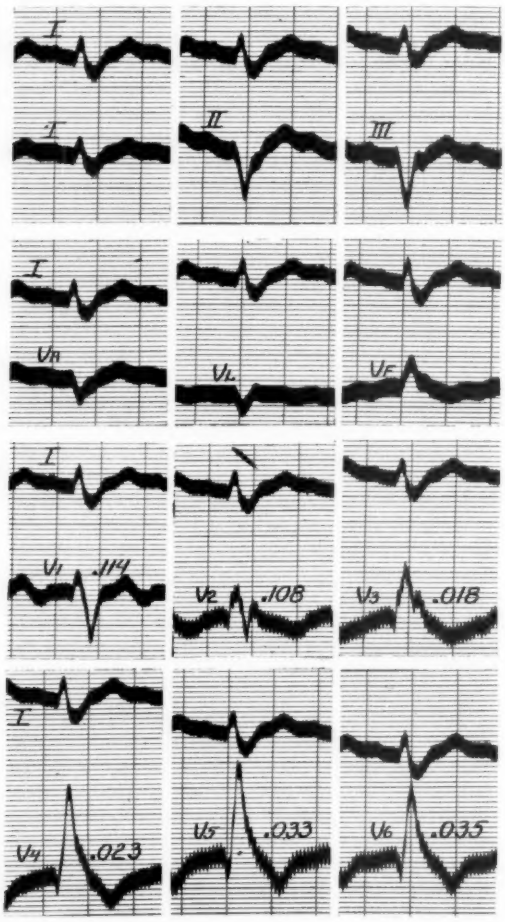

Fig. 3.—Case 3. QRS interval, 0.153 second. The upper curve of each record is standard Lead I. The notes that follow refer to the lower curves only. I, standard Lead I; II, standard Lead II; III, standard Lead III. V_R, potential variations of the right arm; V_L, potential variations of the left arm; V_F, potential variations of the left leg. The last six curves represent the potential variations of the following precordial points: V_1, fourth rib at right edge of sternum; V_2, fourth interspace at left edge of sternum; V_3, fifth rib halfway between left sternal edge and left nipple line; V_4, fifth interspace left nipple line (apex); V_5, sixth rib left anterior axillary line; V_6, sixth rib left midaxillary line. All of these curves were taken with the galvanometer at the normal sensitivity. The figures written on the records give the interval from the first ventricular deflection in Lead I to the beginning of the chief upstroke of QRS in the lower curve.

minute). A third taken on the following day shows frequent auricular extrasystoles; the sinus rate is approximately 100 per minute. A fourth taken four days before death shows auricular fibrillation. In all of these curves the ventricular complexes of the sequential beats are of the same form and suggest high grade intraventricular block (Fig. 3).

The autopsy showed bilateral thrombosis of the great saphenous veins, more recent on the left side, with secondary pulmonary embolism. There were many infarcts in the lungs, and this was apparently the immediate cause of death. The heart weighed 500 grams; its position in the body was not noticeably unusual. No areas of fibrosis were visible to the naked eye. On the left side of the lower septum there was a questionable change in the color of the muscle; it seemed slightly paler than the rest of the myocardium. The valves were not abnormal. The larger coronary vessels showed patchy atherosclerosis but no thrombi were found.

Microscopic examination of the heart muscle showed hypertrophy of the fibers and pronounced atherosclerosis of the coronary arteries with calcification of the media and narrowing of the lumen. There were numerous areas of fibrosis and a small area of recent softening was also seen. The areas of fibrosis were most conspicuous in the septum, and here there was also some localized impairment of the staining power of the muscle, suggesting early ischemic necrosis. The latter change was slightly more pronounced in some of the blocks from the free wall of the left ventricle.

The electrocardiograms shown in Fig. 3 were taken nine days before death. The standard curves are similar to those shown in Figs. 1 and 2. The QRS interval is approximately 0.153 second. In Lead I the ventricular deflections are small, the R and S deflections are of about the same size, but the latter is the broader. In Leads II and III, R is very small and S very deep and broad. The first precordial curve is similar to the corresponding curves of Figs. 1 and 2. The chief upstroke of QRS is late and begins about 0.1 second after the onset of R in Lead III. In the curves from the left side of the precordium the chief upstroke of QRS is early; it begins 0.02 to 0.03 second after the onset of R in Lead I. The second precordial curve is of the kind we have referred to as transitional.[1]

DISCUSSION

The standard electrocardiograms in these three cases resemble some of those that have been obtained after section of the right branch of the His bundle in the dog. Right branch block in this animal is almost always represented by curves in which all the ventricular deflections of Lead I are small; in some instances R and in others S is the more prominent. In Leads II and III the chief and final deflection of the QRS group is downward. So far as Lead I is concerned, the standard curves reproduced in this article are also somewhat like those in which the ventricular complexes show a broad S-deflection in Lead I and a simultaneous broad upward movement in Lead III.[2] In the latter, however, the deflections of Lead I are larger; R is thinner and more prominent, and T is more definitely upright than in the former; S is conspicuous in both. The resemblance does not extend to Leads II and III; in these leads curves of the former kind are more like and cannot be easily distinguished from those that are seen in left branch block.

The precordial curves indicate clearly that in each instance the conduction defect was on the right side. They are similar to those obtained in right branch block in the dog and to those obtained in patients who exhibit diphasic ventricular complexes of the rare type or ventricular complexes with broad S deflections in Lead I.[2] There are certain minor differences, which may or may not be important. In Cases 1 and 2 the areas from which complexes showing a late upstroke were obtained was much larger and extended much further to the left than is usual; this is not true, however, of Case 3. The curves from the left side of the precordium lack the deep downward movement at the beginning of the QRS interval that ordinarily occurs in the same leads in normal subjects, in dogs with right branch block and in most of the patients with electrocardiograms of the kind we attribute to right branch block. In the first two cases the chief upstroke of QRS is unusually small and of unusually long duration.

It is possible that in cases of the kind described in this paper we are dealing with right branch block plus something else that modifies the ventricular complexes of the standard leads and of leads from the left side of the precordium. This additional factor, if it is really present, need not always be the same. In some cases it may be some peculiarity in the position of the heart; in others a lesion of some of the subdivisions of the left bundle-branch or infarction of the free or septal wall of the left ventricle. In Case 3 the extensive changes in the coronaries and in the left ventricular muscle found at autopsy may have played some part in determining the unusual outline of the electrocardiogram. In the other cases widespread myocardial changes were probably present, but there were no symptoms or signs suggesting myocardial infarction.

Electrocardiograms of the kind under consideration do not appear to be very common, but their real frequency is as yet unknown. An electrocardiogram that probably belongs to this class was reproduced in a recent article from this laboratory[4] (see Fig. 20 *D*, p. 195). It was there mistakenly referred to as an atypical example of the curves seen in branch block of the common type. A large infarct involving the apical portion of the left ventricle was found post-mortem. Another curve of the same kind is reproduced in Mahaim's[5] treatise on lesions of the His bundle (his Fig. 72, p. 242). In this instance embolic obstruction of the anterior descending branch of the left coronary artery was found at autopsy. The infarct was on the anterior and septal wall of the left ventricle. Serial sections of the bundle-branches showed lesions interrupting the right branch and the anterior subdivisions of the left. It may be pointed out that the curves reproduced in Figs. 89, 95, and 100 of Mahaim's work also show conspicuous S deflections in Lead I. In this respect they are like those reproduced in this article, and quite different from curves of the kind

we attribute to left branch block. A search of the literature would undoubtedly disclose other cases in which curves of the type under consideration were recorded (see Pardee,[6] Fig. 18 *A*, p. 76).

SUMMARY

There are certain cases of intraventricular block in which the ventricular complexes of the electrocardiograms show the following characteristics: In Lead I all the ventricular deflections are small. There is a conspicuous S deflection, and T is usually flat or upright. In Leads II and III the ventricular deflections are similar in all respects to those seen in bundle-branch block of the common variety.

Precordial leads have been employed in three cases in which the standard electrocardiograms were of this kind. In these leads the ventricular complexes are like those that are recorded in dogs with right branch block and in patients with diphasic ventricular complexes of the rare type. It is thought that the curves referred to represent right branch block. Some additional factor that modifies the form of the electrocardiogram may be present.

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PRIMARY SARCOMA OF THE HEART

Report of a Case With Electrocardiographic and Pathological Studies*†

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INVASION of the heart by a neoplastic process, whether primary or secondary, is relatively rare. Lymburner, in a review of 8,550 postmortem examinations at The Mayo Clinic, found 4 cases of primary tumor of the heart, and in 52 cases the heart was the site of metastatic invasion by neoplasms. Adami stated that the relative immunity of the heart to neoplastic involvement "is probably to be attributed to the fact that the heart, above all organs, is constantly in a state of great efficiency, well-nourished, well-innervated, and functionally always active." The rarity of cardiac neoplasms is attested by the fact that Lymburner found only 226 cases of primary tumors of the heart recorded in the literature, to which he added 4 cases. The first reports of cases are attributed, by Beck and Thatcher, to Zollicofferus (1685) and Theophy Boneti (1700). According to Perlstein, the first authentic modern cases are those of Albers (1835) and Bodenheimer (1865). In recent years, a number of writers have reported additional cases and have reviewed the literature; among the more important reviews of this type are those of Perlstein, Beck and Thatcher, Meroz, Uehlinger, Karrenstein, Goldstein, Bradley and Maxwell, Diebold, Pommer, and Matras. The consensus of opinion of these writers is that the majority of primary cardiac tumors are of mesenchymal origin, and may be classified as spindle-cell, round-cell or mixed-cell sarcomas, the first-named being the type most commonly encountered; a few rhabdomyosarcomas have also been noted. The primary focus of these tumors is variable. Beck and Thatcher cited Link's series of cases, and noted the relatively high incidence of primary involvement of the auricles; the ventricles, valves, and intra-auricular septum are considerably less common as primary sites.

The symptoms of these tumors are, as one might expect, as variable as is their distribution. Numerous analyses of the symptoms have been made, but no constant clinical syndrome can be said to have been established. As Meroz has pointed out, there can be no characteristic symptoms if the tumor does not interfere with the cardiac mechanism.

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He went on to state that if the valve orifices are involved, stenosis, regurgitation, or both, may result, and the pulmonary and general circulation may be involved singly or in combination. If the pericardial surface is involved, an effusion, usually hemorrhagic, results; involvement of the cavities may produce multiple embolic phenomena, and involvement of the conduction system may produce arrhythmia of various types. Meroz' conception of the symptoms of cardiac tumors is based chiefly on hypothetical grounds. Nowicki, Bradley and Maxwell, Matras, and others, from a study of case records, have outlined the symptoms most commonly recorded in the literature. Among these may be mentioned: (1) progressive circulatory failure, for which no obvious anatomical basis can be demonstrated; (2) progressively increasing valvular stenosis, with murmurs which change on movement or from day to day; (3) signs of mediastinal tumor, sometimes associated with gross changes in the appearance of the heart on roentgenological examination; and (4) recurrent hemorrhagic pericardial or pleural effusions.

So far as we are able to judge from available reports in the literature, the diagnosis of a primary cardiac neoplasm has not been made during life. Lymburner reviewed 4 cases in which secondary tumors of the heart had been recognized during life, including the case reported by Willius and Amberg in 1921. The case reported here is of particular interest because the coexistence of signs of pericarditis, heart-block, and metastasis to the muscles of the shoulder girdle permitted a tentative clinical diagnosis of malignant involvement of the heart. Curiously enough, the two principal diagnostic points in this case, heart-block and metastasis to the skeletal system, appear to be particularly uncommon. Bradley and Maxwell stated that heart-block has been noted in two cases, and Goldstein cited the case of Armstrong and Monckeberg, in which this condition developed in an infant with a cardiac tumor. In Beck and Thatcher's case a metastatic deposit was noted in the right deltoid muscle. In Perlstein's series of thirty cases, metastasis was noted in the lungs, liver, pancreas, and mediastinal lymph nodes, and in the suprarenal glands, but not in the skeletal system. The diagnosis in this case is therefore no contradiction of the often-quoted statement that diagnosis of a cardiac tumor is "either impossible or a matter of good fortune."

CASE REPORT

A woman, a housekeeper, aged sixty-two years, was admitted to St. Mary's Hospital December 10, 1932, because of pain in the thorax and dyspnea on exertion. These symptoms had been present for about two months and had been accompanied by definite loss of weight and strength. For about one month she had suffered from night sweats, and was known to have had a daily rise in temperature to 100° or 102° F. The past history was entirely irrelevant to the complaint at the time of admission.

Physical examination gave evidence of considerable loss of weight, and the patient was decidedly ill. The temperature was 102° F., and the pulse rate 120 beats each minute. Cyanosis or peripheral edema could not be made out, but definite orthopnea was present. There were no oral foci. Examination of the lungs gave essentially negative results. There were no significant abdominal findings, except some tenderness in the upper end of a previous laparotomy scar. Examination of the pelvis gave essentially negative results, except for evidence of menopausal involutionary change. The principal physical findings concerned the heart. It was not enlarged, the tones were clear, and definite valvular murmurs could not be heard. Loud friction sounds were heard all over the precordium, varying somewhat on change in the patient's condition. Results of urinalysis and serological test for syphilis were negative. The concentration of hemoglobin was 11.4 gm.; erythrocytes numbered 4,390,000 and leucocytes 6,200 in each cubic millimeter of blood. A roentgenogram of the thorax revealed a calcified tuberculous process in the upper lobe of the left lung. Two cultures of the blood did not reveal growth in forty-eight hours. An agglutination test for *Alcaligenes abortus* was negative. Electrocardiographic examination disclosed a rate of 106, sinus tachycardia, exaggerated P-wave in derivation II, and slurred QRS complexes in derivations II and III.

A diagnosis of subacute, fibrinous pericarditis was made, but no explanation was advanced at the time as to its etiology. Because of its probable infectious nature, however, a course of sodium cacodylate was begun, the dosage consisting of 7½ grains (0.48 gm.) given intravenously twice daily. Five days later the pericardial friction sounds were altered; in fact, with the patient in the sitting position they were almost inaudible. There were no signs of pericardial effusion, and she was definitely better. December 22 the pericardial friction sounds had completely disappeared, and the temperature remained below 100° F. for twenty-four hours. Administration of sodium cacodylate was discontinued at this time. On this date the pain in the thorax was entirely relieved, but on December 26 it reappeared, and the temperature began to become elevated in the afternoon to about 102° F. Another course of sodium cacodylate was begun, but within three days a diffuse, arsenical type of dermatitis developed, which compelled us to abandon this form of treatment. The dermatitis cleared rapidly under treatment, and caused the patient no serious inconvenience.

On January 3, 1933, it was noticed that the cardiac tones were much less distinct, especially in the region of the apex. There were no definite signs of pericardial effusion, and roentgenograms of the thorax did not reveal significant widening of the cardiac shadow. An electrocardiogram made on this date revealed a rate of 116, left ventricular preponderance, diphasic T-wave in derivations I and II, notched P-wave in derivation II, and notched QRS complexes in derivation III. Culture of the blood did not reveal growth in forty-eight hours.

On the night of January 5 acute pain developed in the region of the right shoulder. On the following morning the joint was painful to touch, and there was a moderate amount of induration along the posterior border of the deltoid muscle. Local treatment with hot packs, and full doses of salicylates given during the next few days failed to have any effect on this condition, and by January 9 the joint was swollen, hot, and indurated. A tentative diagnosis of metastatic abscess of the right deltoid muscle was made, and after a further period of observation of three days, the muscle was incised under procaine anesthesia. The muscular substance was edematous and indurated, but a definite abscess could not be found. Tissue cultures were made; and a specimen was removed for biopsy. On pathological examination this revealed very evident involvement of the muscle with malignant cells, but these were so un-

differentiated that a definite conclusion could not be reached as to their probable source. The cultures did not reveal growth of organisms. During the next four or five days there was little change in the patient's condition. The pain in the thorax and shoulder continued, and the pericardial friction sounds continued to be definitely audible at times and absent at others.

On the morning of January 18 considerable edema was present in the left arm, the lumbodorsal region, and both lower extremities. The cardiac rhythm, which previously had been regular, was greatly altered, and gross irregularity was noted. An electrocardiogram was made at once, and this gave evidence of an auricular rate of 116 and a ventricular rate of 86, with complete auriculoventricular dissociation. On the following day the cardiac rhythm became regular, but the electrocardiogram revealed a prolonged auriculoventricular conduction time of 0.32 seconds. A diagnosis of tumor of the heart, with involvement of the conduction system and pericardium, and with metastasis to the right deltoid muscle was suggested. Because of the uncertainty with regard to the previous biopsy, another specimen was taken from the same region. A somewhat more satisfactory biopsy was obtained from the muscle, which on examination revealed a highly undifferentiated, infiltrating, degenerating cellular tumor, probably a sarcoma. This development appeared to establish definitely the diagnosis of sarcomatous involvement of the heart. Owing to the patient's greatly weakened condition the search for a primary source was necessarily curtailed, and the results were entirely negative. Repeated roentgenological examinations of the thorax and a series of cultures of the blood gave no significant results. Electrocardiograms were made January 21, 23, 25, and 27, all of them giving evidence of complete auriculoventricular dissociation. The peripheral edema, which had been noted previously, increased slowly. The patient became more and more stuporous, and roused only to complain of pain in the affected shoulder. She took almost no food, and appeared to fail very rapidly. A course of radium therapy was given over the right shoulder in the hope of relieving the pain and perhaps of effecting slight temporary improvement in her general condition. She was transferred to her home by ambulance January 31, when the treatment with radium had been completed. Her course there was marked by progressive failure and increasing edema and orthopnea, as well as by other signs of circulatory failure. Death occurred February 14. Examination shortly before death gave no further clinical evidence of sarcomatosis, except some rather questionable nodules in the region of the left deltoid muscle.

Necropsy.—Necropsy was performed five hours after death. The body was extremely emaciated, and the lower extremities were markedly edematous. Multiple purpuric patches were present on the skin of the face and forehead. The skin of the right arm, overlying the deltoid muscle, was thickened and revealed multiple firm, fixed, small, shotlike, subcutaneous nodules, by palpation. In both pleural cavities there was clear, dark amber fluid, 500 c.c. in the right cavity and 1,000 c.c. in the left. The pericardial cavity was obliterated, partially by fibrous and fibrinous adhesions between the parietal and visceral layers, but also by the interposition of soft, grayish white, neoplastic tissue. The neoplastic tissue appeared to arise from both parietal and visceral layers, and to be entirely confined within the sac; the external surface of the parietal pericardium was smooth, glistening, and apparently free from tumorous involvement. On manual separation of the pericardial surfaces, the internal parietal surface and the visceral surface disclosed multiple grayish white, relatively soft, slightly elevated, plaque-like masses of tissue. These were so numerous that diffuse involvement was approximated, but where discrete, these areas were from 2 mm. to 5 mm. in irregular diameter (Fig. 1).

The heart and adherent pericardium weighed 325 gm. The wall of the right auricle was diffusely thickened and replaced by relatively soft, friable, grayish white tissue, which was contiguous with similar appearing tissue of the epicardium. Although the auricular wall appeared to be diffusely involved, there were some areas which were distinctly nodular. These were especially prominent above the posterior cusp of the tricuspid valve, where the endocardium was eroded by tumor. Here the tumor extended somewhat into the auricular chamber, as slightly elevated and roughened nodules; the two largest of these were each 1 cm. in diameter. Elsewhere the endocardium of the auricle was smooth and apparently not extensively invaded; where considerable tumor tissue existed in the wall, however, there was an evenly rounded bulging of the corresponding portion of the wall toward the auricular chamber. This was especially the case in the region of the interauricular septum, below the foramen ovale. The thickness of the wall of the right auricle was usually 0.5 to 1.5 cm., but at the septum it was 2.5 cm. thick. The tricuspid

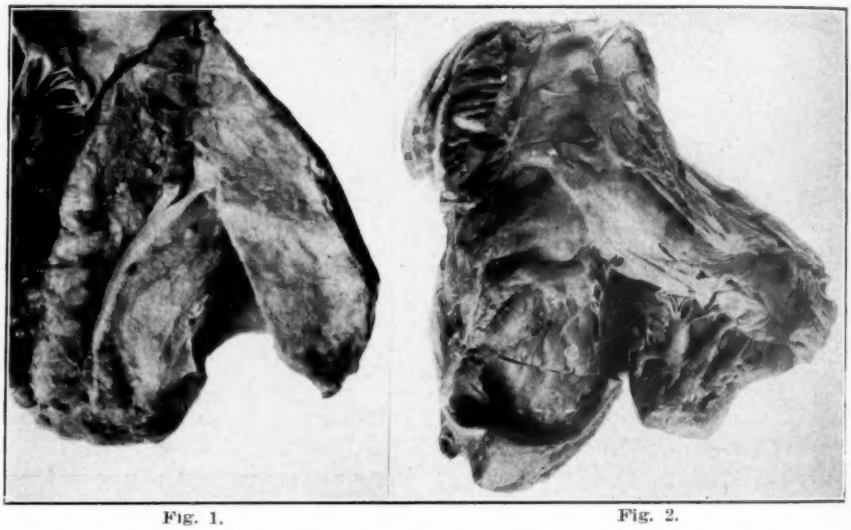


Fig. 1. Fig. 2.

Fig. 1.—Neoplastic involvement of the pericardium over the posterior portion of the left ventricle. The pericardium has been reflected from the epicardium.

Fig. 2.—Involvement of the right auricle and right ventricle by the neoplasm. The tumor of the auricle is particularly prominent above the tricuspid valves. Most extensive involvement of the right ventricle appears on the interventricular wall; an incision appears through the center of this area.

valves were normal. The wall of the right ventricle was involved in a way similar to that of the right auricle, but the involvement was less extensive. There was diffuse, grayish white, neoplastic infiltration of the ventricular muscle below the posterior papillary muscle, extending downward to the apex, and anteriorly to the base of the anterior papillary muscle; the tumor extended toward the left in the interventricular septal portion of the right ventricle, as far as the papillary muscle of the conus. Most of the neoplastic change observed in the right ventricle was in this portion. There was no tumor observable in the anterior wall (except near the apex) in the region of the conus arteriosus, in the base beneath the tricuspid valves, nor in the extreme left portion of the septal region. At the apex, the wall of the right ventricle was 1.5 cm. thick; elsewhere the thickness averaged 0.8 cm. Nowhere in the right ventricle did the tumor extend through the endocardium. The

pulmonary valves were normal. (Fig. 2.) The left auricular wall was invaded by neoplasm only in the region of the interauricular septum and the auricular appendage. The wall of the appendage was 1 cm. thick. Elsewhere, except in the interauricular septum, the wall of the left auricle was 1 to 2 mm. thick. The mitral valves were normal. The left ventricle was normal; its muscle was approximately 1 cm. thick. The aortic valves were normal. The large vessels, to and from the heart, were normal, without neoplasm surrounding them, except in their intrapericardial portion.

Both lungs revealed numerous very small, mostly subpleural, metastatic nodules, the largest of which was 1.5 cm. in diameter. The thymus gland was replaced by adipose tissue; there were no metastatic nodules. About the arch of the aorta, and the bifurcation of the trachea, some lymph nodes were enlarged. In one region the nodes were conglomerate and formed a firm, grayish white mass 3 cm. in diameter. Lymph nodes elsewhere were somewhat enlarged, but on gross inspection disclosed

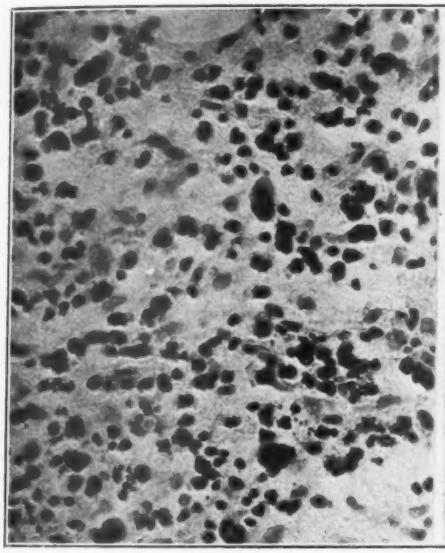


Fig. 3.

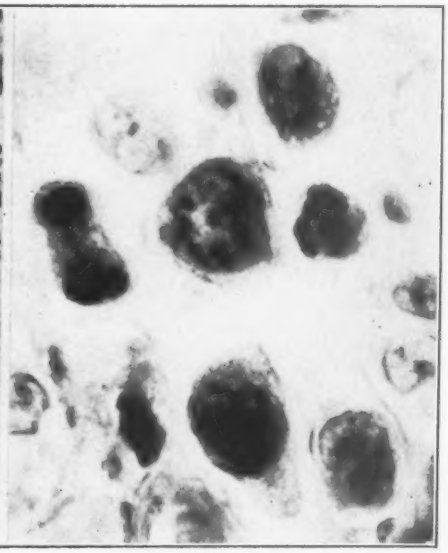


Fig. 4.

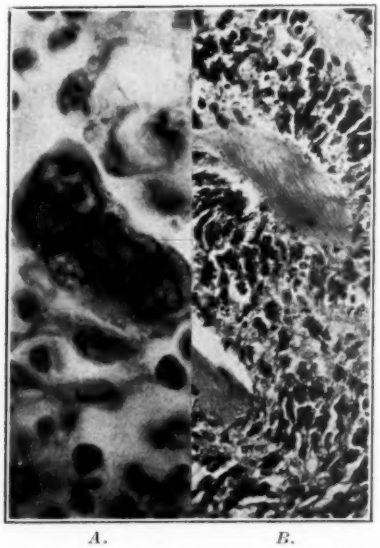
Fig. 3.—The polymorphism of the tumor, as it involves the epicardium of the right auricle, may be seen. Large cells with abundant cytoplasm, others with tendency to spindle formation, especially in the background, may be noted (hematoxylin and eosin, ×365).

Fig. 4.—Mediastinal lymph node. Cells with abundant reticulated cytoplasm, and small cytoplasmic vacuoles (Mallory's phosphotungstic acid hematoxylin, ×1875).

no evidence of tumor. The thyroid gland was atrophic, but otherwise revealed no lesions. The cervical nodes were not remarkable in any way. The esophagus, stomach and intestinal tract were normal. The pancreas was normal, except for one firm pinkish white nodule 0.5 cm. in diameter in the body of the gland. There was one metastatic nodule 1 cm. in diameter in the liver. The spleen was normal. The left suprarenal gland was enlarged and appeared to be diffusely involved by an infiltrative type of neoplastic process without loss of identifiable units of the gland. The right suprarenal gland was similar, but revealed only a small fragment of tumor. There were no metastatic growths in the kidneys. The left kidney was atrophic, and weighed 30 gm., apparently representing old, healed pyelonephritis. The right kidney was correspondingly enlarged, and weighed 200 gm.; it was essen-

tially normal. Except for left cystic pyelitis and ureteritis, the remainder of the urinary tract was normal. There were multiple, small, subserous leiomyomas in the uterus. The adnexa were normal. The brain was not examined.

Microscopic sections of the tumor, taken from the pericardium and myocardium, revealed a highly malignant neoplasm of polymorphous cell type. In the myocardium the tumor cells tended to invade the muscle-bundle interspaces, but occasionally large aggregations of tumor cells were formed, from which cardiac muscle cells had entirely disappeared. Both pericardium and epicardium were involved by the tumor, and the normal spaces between these structures were obliterated by tumor and organizing fibrinous exudate. The neoplastic cells were usually large and spherical or oval, with some tendency to long spindle shapes (Fig. 3). The smaller cells resembled lymphocytes, although they were somewhat larger. In these, there was usually a scant amount of cytoplasm. In the cells of greater size the cytoplasm was abundant, and had marked affinity for the eosin stain. The cytoplasm of the larger cells was sometimes foamy, due to small, unstained vacuoles (Fig. 4). In other cells a fine, reticular, cytoplasmic structure was identified. This sometimes, by use of Mallory's



A. *B.*

Fig. 5.—*A*, Mediastinal lymph node. Giant cell with abundant cytoplasm and multiple nuclei. Faint longitudinal fibrillae and rows of evenly placed granules resembling embryonic sarcous elements or striations may also be seen faintly in the cytoplasm (Mallory's phosphotungstic acid hematoxylin, ×1250). *B*, Biopsy revealed metastasis to deltoid muscle. Polymorphous character of cells with many oval or spindle forms may be noted (hematoxylin and eosin, ×250).

phosphotungstic-acid hematoxylin stain, was revealed as very fine, scarcely visible longitudinal fibrillae, with more deeply stained granules in dotlike lines. These suggested concentration points of embryonal sarcous elements, the striations of embryonic muscle cells (Fig. 5*A*). Nuclei of the tumor cells were usually large, hyperchromatic structures, often with finely divided chromatin. This gave some nuclei the appearance of a meshwork of chromatin. Some cells had two or three large nuclei. Mitotic figures were fairly numerous. Cells were often undergoing retrogressive changes, and in these the nuclei were in a state of karyorrhexis. In several portions of the tumor necrosis was advanced. This was especially the case in the epicardium. Lymphocytes and polymorphonuclear neutrophilic leucocytes were collected in aggregations, particularly in the epicardium and pericardium, and at

the periphery of necrotic portions of the tumor. Vessels of the epicardium and myocardium were often surrounded by tumor cells, and some of them contained cells of similar appearance which packed their lumina. Metastatic involvement was proved to be present, by microscopic sections, in the right deltoid muscle (two specimens for biopsy; Fig. 5*B*), lungs, liver, suprarenal glands and lymph nodes (mediastinal, aortic and mesenteric). In all of these the morphological characteristics of the cells were either identical with or similar to those observed in the heart and pericardium. The extreme degrees of polymorphism which were disclosed by the tumor in the pericardium and myocardium were exhibited less frequently by the metastatic growths; however, marked variations in size, shape and staining of the cells did occur. The metastatic growths in the deltoid muscle, mediastinal lymph nodes, and lungs, as in portions of the cardiac tumor, revealed extreme degrees of necrosis; however, there were always areas of preserved cells near the periphery of the growth. In the aortic and mesenteric lymph nodes, and in the suprarenal glands, the tumor cells were evidently young and well preserved, and offered excellent opportunity for detailed study of individual cells. In all situations about the tumors, the blood vessels appeared to be invaded, and in sections elsewhere, such as in the preparations of the leiomyomas of the uterus, tumor cells were often seen packing the lumina of the vessels. The nodule described in the body of the pancreas proved to be an adenoma composed of cells derived from islands of Langerhans.

The anatomical diagnosis was rhabdomyosarcoma, primary in the heart, with metastatic involvement of the pericardium, right deltoid muscle, liver, lungs, suprarenal glands, and lymph nodes.

COMMENT

Electrocardiography.—The electrocardiographic findings in this case, in conjunction with the specimen of muscle removed for biopsy, furnished the key to the correct diagnosis. The sudden appearance of complete auriculoventricular dissociation when previous electrocardiograms had not indicated any disturbance of conduction, suggested that the malignant process which had invaded the deltoid muscle had also invaded the bundle of His. There was no way of knowing, during life, that the malignant process was primary in the heart.

The electrocardiogram in the case reported by Willius and Amberg, mentioned in the early part of this paper, revealed incomplete bundle-branch block of a type indicating involvement of the right bundle-branch (new terminology). This electrocardiographic change is entirely consistent with the fact that the only portion of the right ventricle that was not involved by the tumor was the right anterior portion of the conus. The RS-T changes present in the tracing could easily be explained by the conduction defect in the right bundle-branch.

Lloyd published the electrocardiogram in a case in which the P-R interval was 0.28 second. At necropsy, a tumor was found in the region of the auriculoventricular node. The electrocardiogram in a case reported by Houck and Bennett was essentially negative except for slight changes in the S-T interval, possibly caused by treatment with digitalis. The tumor in this case involved the left auricle.

In the electrocardiogram published by Siegel and Young, the T-waves were inverted in all leads, and the RS-T contours were convex in all leads. There was no evidence of defects of conduction in the tracing. One of us (Barnes) has seen an almost exact replica of this tracing develop a few weeks after occlusion of the anterior descending branch of the left coronary artery complicated by extensive pericarditis. It is interesting to note that Siegel and Young found that the tumor involved an area of the left ventricle, corresponding to that involved by infarction when the descending branch of the left coronary artery is occluded; but they also recorded invasion of the epicardium of the posterior surface of the heart by the tumor. This might correspond to the epicardial involvement observed in the case of coronary occlusion just cited as having been encountered by one of us. The epicardial involvement also might account for the close similarity of the tracings in the two cases. It is our belief that a tumor invading the left ventricle, that does not involve either bundle-branch if localized to the anterior apical or the posterior basal portion of that ventricle, would produce an electrocardiogram which is similar to that obtained in the stage of fibrosis subsequent to acute myocardial infarction. Elevation of the level of take-off of the RS-T segment would not be anticipated from tumorous invasion of the left ventricle, for the acute cellular and vascular reaction which follows acute myocardial infarction is lacking. Likewise, a changing RS-T segment, as seen in acute myocardial infarction, would not be expected in a tumor of the left ventricle, for these RS-T changes in acute infarction are associated with a rapidly changing cellular reaction. This point is well illustrated in the case reported by Siegel and Young.

On the basis of published tracings and on theoretical grounds, it is to be anticipated that most of the electrocardiographic changes that will be observed in cases of tumor of the heart will result from neoplastic invasion of the ventricles. It is probable that invasion of the conducting systems will account for a majority of abnormal electrocardiograms. Because of the much more frequent invasion by tumors of the right ventricle than of the left, right bundle-branch defects should exceed those of the left bundle-branch. Invasion of the muscle of the left ventricle without involvement of the bundle-branches or of the pericardium should produce tracings closely similar to those obtained in the fibrotic stage following acute myocardial infarction. Invasion of the epicardium, either alone or in conjunction with involvement of the ventricles, may produce or modify changes in the waves.[3, 7] If a patient, known to have or to have had a neoplasm, more or less suddenly exhibits these electrocardiographic changes in the absence of any other pathological process in the heart to explain them, then they constitute important presumptive evidence that the malignant process has invaded the heart.

Pathology.—As we have stated previously, primary sarcoma of the heart is a pathological rarity. Perlstein, in 1918, by careful selection, admitted thirty cases of this condition from a compilation of the literature, and added an additional case. Lymburner recently (1933) reviewed the literature exhaustively, and was able to collect fifty-seven cases. Primary sarcomas of the heart have been designated as spindle-celled, giant cell, lymphosarcoma, round-celled sarcoma, mixed-cell sarcoma, fibrosarcoma or myxosarcoma, in agreement with the histological details presented by the cellular constituents of the tumors. Apparently the diagnosis of rhabdomyosarcoma has been made only once, this in a case reported by Bradley and Maxwell, in 1928.

Primary rhabdomyoma of the heart has been less often diagnosed, according to reports in the literature. Of this type of tumor, Lymburner could find only forty-seven examples, and added another case. Primary cardiac rhabdomyomas are considered to be benign tumors, in the sense that in none of the examples referred to in the literature have metastatic growths been noted, although they have been multiple in the heart. Rhabdomyomas predominate in the early years of life. Of the 48 cases collected by Lymburner, 20 occurred within the first year of life, and only 5 between the twentieth and forty-fifth years. Rhabdomyomas of the heart have a further distinctive characteristic in being associated frequently with functional or anatomical developmental defects, epilepsy and tuberous sclerosis of the brain being the two most common of many such disturbances which have been found. It is believed that rhabdomyomas are an expression of abnormal tissue differentiation, or represent secondary developments from embryonic tissue rests. They present a characteristic microscopic picture, in which the large, irregularly processed and vacuolated, so-called "spider cells," and long spindle cells with delicate longitudinal fibrillae and cross striae form the essential differential points. The cells frequently contain excess glycogen.

The relationship which the typical rhabdomyoma of the heart might bear to primary sarcoma of the heart is difficult or impossible to ascertain accurately, since only once has the differentiation in sarcoma been considered sufficient to admit the diagnosis, primary rhabdomyosarcoma. From a more or less superficial survey of the field, it would appear that the two types of tumor are distinct, and with possible exceptions, it seems improbable that primary sarcoma of the heart arises from malignant transformations of a rhabdomyoma. Transitional stages apparently do not exist, for as Lymburner remarked: "All reported cases (of rhabdomyoma) seemed to possess a similar microscopic appearance, regardless of the age of the patient, and evidently had obtained their final development in embryonic life." Primary sarcomas and rhabdomyomas of the heart are further distin-

guished in that they appear in different age groups. Although cardiac rhabdomyomas predominate among young people, cardiac sarcomas predominate among middle-aged and older people; only two cases have been recorded in which the patients were less than twenty years of age. Also, primary sarcomas are not associated with developmental defects, whereas rhabdomyomas usually are.

In reviewing cases reported in the literature, we have found that there was one which strikingly resembled the case reported here. The case was described by Bradley and Maxwell. Their patient was a man, aged sixty-two years; his clinical history was similar to that recorded for our patient. The gross and microscopic appearances of the tumor in each case were similar, although not identical. The histological differentiation of the tumor described by Bradley and Maxwell was as a polymorphous cell sarcoma with many long spindle cells revealing fibrillae and acidophilic cytoplasm. Sections of the tumor were submitted by Bradley and Maxwell to Mallory, Ewing and Broders. All concurred in the diagnosis of rhabdomyosarcoma.

We have concluded,* as Bradley and Maxwell did in their case, that the diagnosis of the tumor in our case should be rhabdomyosarcoma, primary in the heart. In proof of this we must necessarily first offer evidence that the tumor was of primary cardiac origin. As evidence we may cite the clinical history, which gave every indication that the patient's illness from beginning to end was cardiac. Further proof of the cardiac origin is offered by the macroscopic findings at necropsy. Relatively speaking, although metastasis had occurred, scarcely any tumor was found outside the heart and pericardium. The pericardium and epicardium were involved throughout, and the right auricle and right ventricle were extensively infiltrated. The metastatic areas were small and nowhere gave the impression of primary sarcoma. Conversely, the cardiac tumor had no resemblance to metastatic tumors of the heart, many examples of which we have seen. Microscopic examination gives additional evidence of the primary cardiac nature of the tumor, by way of its histological differentiation. The cells of the tumor were extremely polymorphous; there were many oval or long spindle forms; the larger cells had abundant acidophilic cytoplasm; in a few cells faint fibrillae and striations were observed. Because of the extreme degree of malignancy, the cells were usually totally undifferentiated. However, there were some, as indicated, which revealed sufficient detail to allow identification of the exceedingly suggestive fibrillae and striations. These could hardly be expected to be so clearly defined as in the slowly growing rhabdomyomas, because of the high degree of malignancy of the tumor. The summation of this evidence, we believe, warrants the conclusion, as previously stated.

*Dr. H. E. Robertson and Dr. A. C. Broders have reviewed the sections of this tumor and have concurred in the diagnosis of rhabdomyosarcoma.

SUMMARY

A case is presented in which a diagnosis of tumor of the heart was made during life. The electrocardiographic abnormalities that have been reported in cases of cardiac tumor are reviewed; in our case, the electrocardiographic changes observed were important in establishing the diagnosis. Careful study of the pathological changes in our case, we believe, permits the conclusion that the tumor was a rhabdomyosarcoma, primary in the heart.

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RUPTURE OF NORMAL CHORDAE TENDINEAE OF THE MITRAL VALVE*

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RUPTURE of one or more chordae tendineae of the heart may occur following infectious lesions in endocarditis or because of lesions of papillary muscles. These are the only responsible conditions recorded by White[1] and by Vaquez[2] in their comprehensive reviews of the literature. If rupture of chordae tendineae under other circumstances has been reported, diligent searchers have not brought it to light. It seems obligatory, therefore, to report a case, probably unique, of rupture of the chordae tendineae in which no disease of these structures or of the papillary muscles could be found. In this case there was calcification in a part of the mitral valve to which the ruptured chordae tendineae were attached. The possible relationship between this calcification and the rupture will be discussed later, but the chordae tendineae at the site of the rupture appeared to be normal.

CASE REPORT

The patient (Medical number 41737), was a man sixty-five years of age. He came to autopsy on April 9, 1933, having been ill in bed since the preceding August. The first weeks of his illness were spent at St. Luke's Hospital in New Bedford and the later months at the Peter Bent Brigham Hospital in Boston. So far as the present problem is concerned, his family history was unimportant. The following data are all that could be collected about his past cardiac history. He had rowed in college for four years on the varsity crew and it may be assumed that his heart was not remarkable during that period as there was then a physician who examined the athletes. When he was forty-six years old, an excellent physician made a note that his heart was "negative excepting for soft first sounds." When he was about sixty-three years of age, another excellent physician examined his heart and found no murmurs. For the year preceding his final illness he was reported as saying that he became somewhat short of breath on exertion so that he could not swim or row so far as formerly. He also said that he had had some cough for the past two years without apparent cause. Otherwise his past history was unimportant. He was a man of excellent habits, and he kept himself physically in good condition and did not become overweight. There was no history of syphilis, and the Wassermann reaction of the blood serum was negative.

His present illness began with an attack of shortness of breath which awakened him from sleep about two o'clock on the morning of August 7, 1932. On the afternoon before, he had rowed a boat for over an hour against wind and unfavorable tide. He did not overexert himself and experienced no dyspnea or weakness. After the row he went swimming and after that walked up a steep hill to his home. So

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far as can be ascertained he did not experience any discomfort during that evening and went to bed without suspicion of anything unusual in his physical condition. When seen by Dr. Russell Wood of New Bedford about three o'clock in the morning he was cyanotic and markedly dyspneic. He had pulmonary edema and tachycardia. Under morphine and atropine he improved rapidly and had several hours' sleep. The dyspnea with pronounced orthopnea continued. On August 12, 1932, he entered St. Luke's Hospital in New Bedford. At this time the physical examination in addition to the orthopnea and cardiac abnormalities showed a few scattered râles in the chest and slight edema of the ankles. The heart appeared somewhat enlarged to percussion. No thrills were felt. The first sound all over the precordia was replaced by a harsh systolic murmur. No diastolic murmurs were heard. The rhythm was normal and the rate slightly accelerated. The blood pressure was 135 systolic over 85 diastolic. What his blood pressure had been before this upset could not be ascertained. The routine clinical pathology was essentially negative. An electrocardiogram taken on August 24, after he had been taking digitalis is reported as showing "heart muscle weakness and digitalis effect." One of the authors (C. F.) saw him on August 26, at which time the conditions were practically the same as described above. The amount of dyspnea and orthopnea seemed out of proportion to the slight amount of edema of the legs and over the sacrum. Furthermore, the edema had been gradually increasing, so that it seemed reasonable to believe that some sudden injury to the heart had occurred, and in consequence cardiac decompensation was gradually developing. The possibility of a coronary occlusion without pain was seriously considered, although the unusually harsh systolic murmur could not be accounted for on this basis. Others thought that there had been gradually increasing myocardial weakness which had been suddenly accentuated by the strenuous day preceding the upset. When seen next by one of the authors (C. F.) on September 3, conditions were practically the same except that the edema of the legs and over the sacrum was more pronounced.

For the remainder of his stay at St. Luke's Hospital the evidence of cardiac decompensation increased slightly despite excellent cooperation on the patient's part and careful nursing. On September 21, he entered the Peter Bent Brigham Hospital, where he remained until his death from a terminal bronchopneumonia on April 9, 1933. The outstanding features of the case during his stay of over six months at the Brigham Hospital were the attempts to develop cardiac compensation and the gradually increasing psychosis. He was practically afebrile during his stay in the Brigham Hospital except for a few days in January and during the terminal infection. His pulse showed a regular rhythm and usually ranged between 80 and 90 beats per minute. Rarely it reached 110 beats per minute, and often it ranged between 70 and 80. Respirations were usually about 20 per minute. Occasionally they went up to 25 but often were about 15.

By the end of September the edema of the legs and over the sacrum had increased; ascites was present and hydrothorax existed on both sides. The liver was also easily palpable, three fingerbreadths below the right costal margin. Late in September Cheyne-Stokes breathing developed and continued until his death. He also began to be disoriented at night. Despite excellent responses to theocin and later salyrgan the dropsy could be only temporarily relieved and the liver remained enlarged. He gradually improved in regard to orthopnea so that he was able to lie back with only three pillows at times. However, it could not be said that his circulation ever became reestablished to normal. The systolic blood pressure during his six and one-half months' stay in the hospital ranged from 160 to 128 and the diastolic from 104 to 76. On January 19 a systolic thrill was felt over the base of the heart when the patient leaned forward, but this did not persist. No other murmurs ever developed and the systolic murmur remained the same.

The patient's mental condition during these six and one-half months ranged from normal to moderate disorientation and irrationality and then to almost active mania.

In the months of February and March he had a few convulsive attacks, the cause for which was not clear, followed by no sequelae. Because of a corneal scar only one eyeground was visible, but this appeared to be normal. In April he developed a bronchopneumonia to which he succumbed in a few days.

The autopsy was performed by one of the authors (G. H.) two and one-half hours after the patient's death. The anatomical diagnoses are as follows: *ruptured chordae tendineae of posterior mitral cusp (healed); calcification of annulus fibrosus of mitral valve (posterior cusp); cardiac dilatation; hydrothorax; ascites; chronic passive congestion of viscera; arteriosclerosis (slight, generalized); bronchopneumonia (immediate cause of death); pleuritis (serofibrinous); hyalinization of islets of Langerhans; cirrhosis of liver; encephalomalacia (focal).*

As the most important lesions were in the heart, the description of that will be given first.

Heart—Gross Appearance.—In the pericardial cavity there were 20 c.c. of clear fluid. The heart, as it lay in situ, was dilated. The right auricle and right ventricle were greatly distended. The left auricle was much less prominent than the right. The left ventricle was relatively contracted. The coronary arteries were neither unusually tortuous nor thick walled. The heart weighed 360 grams. The measurements of the circumference of three valvular orifices were as follows: tricuspid, 14 cm.; pulmonary, 8 cm.; and aortic, 7.5 cm. The cusps, chordae tendineae and papillary muscles of these valves were essentially normal.

The mitral valve and its annulus fibrosus, chordae tendineae and papillary muscles were the seat of the only significant pathological changes in the heart. The orifice easily admitted the passage of two fingers. When viewed from the auricular side, it was noted that the middle three-fifths of the posterior cusp bulged upward into the mitral opening. The valve ring was not disturbed, and the left ventricle was carefully opened by a lateral incision which was carried through the ventricular wall between the anterior and posterior groups of papillary muscles. As was suspected, the middle one-third of the posterior cusp was almost entirely free from its attachments to the papillary muscles. Four ruptured chordae tendineae were found. The distal portions were traced for distances of from 2 to 10 mm. to points where they branched into fibrous cords, which were attached either to the free margin or to the ventricular surface of the middle one-third of the posterior cusp. The proximal portions of the four ruptured chordae were from 2 to 10 mm. in length. Three were attached to the posterior group of papillary muscles and one to the anterior group. The free ends were tapered smooth and rounded. The remnants of the chordae were slightly contracted and atrophic. There were no apparent gross defects in the structure of either the chordae which had ruptured or those which had preserved their usual continuity. Except for slight atrophy of the musculature adjacent to the attachment of the ruptured chordae tendineae, the papillary muscles were normal. Although there was slight bluntness of the free margin of the middle portion of the posterior cusp, the cusps of the mitral valve were essentially normal. There was no evidence of either a healed or active endocarditis involving the valve leaflets or chordae tendineae. However, in the annulus fibrosus there were irregular masses of calcium which extended for from 1 to 3 mm. into the substance of the valve at its attachment. Of greatest significance was the restriction of these calcific deposits to the annulus fibrosis of the posterior cusp, especially at the attachment of that portion of the leaflet which was affected by the rupture of the chordae tendineae.

The musculature of the left ventricle was from 15 to 17 mm. in thickness and that of the right ventricle 4 mm. Numerous incisions disclosed no pathological

changes. The orifices and lumina of the coronary arteries were not narrowed. Only a few slightly elevated atheromatous plaques were encountered in the intima of these vessels.

Heart—Microscopic Study.—The individual muscle fibers showed no degenerative changes and there were no cicatrices. The walls of scattered arterioles were slightly thickened and hyalinized. The intima of the medium-sized coronary arteries was slightly thicker than normal.

Chordae Tendineae: Serial sections were made through three of the ruptured chordae and several of the adjacent intact chordae tendineae. It was concluded after

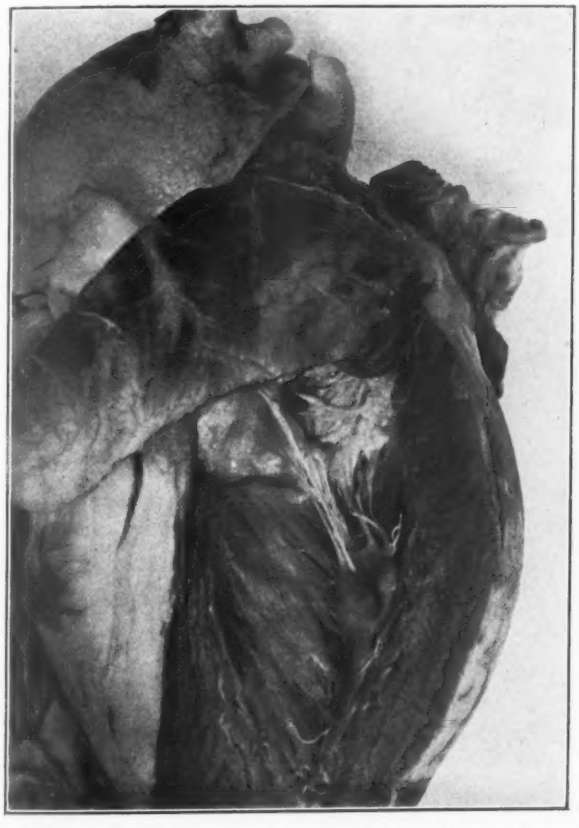

Fig. 1.—Photograph illustrating ruptured chordae tendineae of posterior cusp of mitral valve and the irregularity at the attachment of the cusp produced by calcification in the annulus fibrosus.

a histological study of the former that the duration of time since the rupture had been sufficient to permit repair of the broken ends. In the tissue adjacent to the points at which the chordae tendineae parted there was no inflammatory reaction or apparent preexisting defect in the structure. Neither were there vegetations. The tissue was composed of dense as well as loose-textured avascular collagen in which stellate and fusiform connective tissue cells were imbedded. Covering the surface of each chorda, even at the point of separation, there was a layer of endothelial cells. The histology of the intact chordae, which were cut in serial sections for the purpose of making control studies, differed from that of the ruptured chordae

tendineae in that the collagen fibrils were arranged in normal, compact, straight, parallel bundles which were of uniform texture.

Papillary Muscles: Sections through the papillary muscles at the origins of the ruptured chordae tendineae were essentially negative except for slight atrophy of the muscle fibers.

Other Organs—Gross Appearance.—The remaining organs on gross inspection showed a few changes worthy of mention. There was evidence of congestion, edema and bronchopneumonia in each lung. In the right pleural cavity there were 1,050 c.c. and in the left 450 c.c. of slightly turbid fluid, which contained a few flakes of fibrin; 100 c.c. of clear watery fluid were found in the peritoneal cavity. The liver weighed 1,870 grams and had a slightly thickened irregular capsule. The parenchyma had the typical mottled appearance of a "nutmeg" liver and a mild cirrhosis, both of which were the result of chronic passive congestion. The spleen weighed 220 grams. There was moderate engorgement but no increase in the amount of stroma.

The right kidney weighed 200 grams and the left kidney 180 grams. The cortical substance measured from 5 to 6 mm. in thickness, and except for small scattered subcapsular scars, the parenchyma of each organ was normal. The pancreas, adrenals, thyroid, prostate and pituitary were normal. The aorta retained much of its elasticity, and there was only slight atherosclerosis. A study of the brain revealed large pacchionian granulations, slight fibrous thickening of the pia-arachnoid, and a small area of softening (2 mm. × 3 mm.) in the left globus pallidus. The lumen of the left lateral sinus was very small.

Microscopic Study of Other Organs.—Lungs: The principal variations from normal histology may be attributed to chronic passive congestion and an acute bronchopneumonia. In many alveolar spaces there were aggregates of mononuclear leucocytes. The majority of these were heavily laden with hemosiderin. The interalveolar septums were doubled in thickness. This was due, not only to distention of capillaries, but also to edema and fibrosis of the stroma. Although an increase in the amount of collagen was most prominent in the alveolar walls, it was also apparent elsewhere, especially in the stroma which supported small and medium-sized blood vessels. This contributed in part to the increased thickness of the walls of veins and arteries. This thickening was due not only to the presence of an unusual amount of collagen in the adventitia, but also to a deposition of similar material in the media and intima. This was especially prominent in the walls of arteries, for in these vessels the intima was thickened, and the smooth muscle was scanty or fragmented. An exudate composed largely of fibrin and polymorphonuclear leucocytes in several alveolar spaces and respiratory passages was the only other significant finding.

Liver: There were moderate changes which were the result of chronic passive congestion. The central veins, the sinusoidal channels and especially the veins in the portal areas were engorged. There was an increase in connective tissue, principally in the portion of the liver which was adjacent to the capsule. The fibrosis was present not only around central veins and adjacent sinusoids but also around the portal structures. The cytoplasm of a few liver cells contained vacuoles which were indicative of a slight degree of fatty metamorphosis.

Spleen: There was moderate hyperplastic sclerosis of the arterioles, dilatation of the sinusoidal spaces, and a slight increase in the amount of connective tissue in the trabecula and between the sinusoids.

Kidneys: The pathological features were not of importance. Hyaline thickening of capillary loops of glomeruli and hyperplastic sclerosis of arterioles were found in the small scattered radial subcapsular cicatrices. These mild changes were considered to be of arteriosclerotic origin.

Pancreas: There was a prominent accumulation of pale, homogeneous or slightly granular, acidophilic hyaline material beneath the endothelium of the capillaries of the islets of Langerhans. Although the distribution of this substance was relatively uniform, in many islets it was of sufficient amount to obliterate the alpha and beta cells. Occasional arterioles showed slight mural hyalinization.

Adrenals: The adrenal cortex and medulla were negative. In the periadrenal tissues there was atrophy of fat, edema of fibro-adipose tissue, and moderate hyperplastic sclerosis of arterioles.

Thyroid: The histology was that of a normal gland.

Prostate: A slight hyperplasia with chronic prostatitis and attendant fibrosis constituted the only findings.

Pituitary: The pars anterior was negative. In the pars intermedia there was a pale, homogeneous or slightly granular material which was located in the walls of capillaries. This deposit closely resembled that which was described in the islets of the pancreas. Small clusters of basophilic cells were found in the pars nervosa adjacent to the pars intermedia.

Aorta: There were very slight variations from normal histology. The fibrils of the intima were increased in number and thickness. Occasionally they were hyalinized, fragmented, and replaced by minute deposits of lipoid.

Brain: Except for a slight increase in the amount of connective tissue of the pia-arachnoid and scattered minute lesions of arteriosclerotic origin, the brain was negative. The increase in collagen in the leptomeninges was no greater than that which is common in individuals of advanced age. Around blood vessels in the cerebrum, just beneath the gray matter of the cortex, there were occasional accumulations of lymphocytes and mononuclear leucocytes. In the latter there were yellow masses of pigment, which, inasmuch as it did not give the iron reaction, was considered to be a lipochrome pigment. In the globus pallidus there was an area of encephalomalacia (2 mm. × 3 mm.). This was characterized by local sclerosis of arteries, degeneration of neural elements, gliosis and accumulations of vacuolated macrophages.

DISCUSSION

The lesions in the brain found at autopsy seemed hardly sufficient to cause the patient's mental disturbance, and it seems fair to say that this was a psychosis due to cardiac decompensation. The cirrhotic changes in the liver were presumably associated with the continued passive congestion. The histology of the lesions in the lungs due to passive congestion was of interest because in this case the events determined the duration of the passive congestion.

The fact that the weight of the heart was within normal limits shows that no appreciable hypertrophy could have existed before the sudden onset of his symptoms, especially as there had been time for some hypertrophy during the long final illness. This fact taken together with the report on the appearance of the myocardium justifies the assumption that the heart was in a satisfactory condition before

the onset of acute symptoms. The strenuous activity which he carried out on the day before the onset of his illness also supports the view that the heart was in good condition and that the slight symptoms of circulatory disturbance which have been mentioned in his past history were of no practical importance. The weight of the heart also justifies the assumption that he did not have an elevated blood pressure previous to his final illness that had persisted long enough to affect his heart. Therefore it seems reasonable to consider that the onset of the cardiac symptoms was associated with the rupture of the chordae tendineae and the subsequent incompetency of the mitral valve. The systolic murmur must have been caused by this incompetency. What little evidence there is points to its absence before his last illness. It is impossible to decide just when the chordae tendineae ruptured, but speculation on this point is interesting. It would be natural for them to rupture during exertion, since the rupture seemed to be purely a mechanical one and not dependent upon disease of the bands. Yet in view of the pronounced cardiac symptoms which developed rapidly and persisted, it would seem as though the onset of the symptoms must have been intimately associated in time with the development of the incompetency of the mitral valve. If such was the case, this incompetency must have developed during sleep and the rupture of the chordae occurred then rather than during the exertions of the afternoon before. Possibly some of the chordae might have ruptured during the exertions of the afternoon and the rupture of the ones which caused the incompetency of the mitral valve happened later from the unusual strain imposed upon them by the rupture of one or more during the exertion.

The histological study shows that there was no acute disease of the ruptured chordae and that except for the rupture and subsequent contraction and atrophy they appeared normal. It also showed that the papillary muscles to which they were attached were not diseased. Apparently, therefore, the rupture was purely a mechanical one, and it hardly seems that a congenital defect would be a factor in a man sixty-four years of age. As described above, in the leaflet of the mitral valve to which the ruptured chordae were attached there was a calcified area at the base, and it seems only reasonable to assume that this calcification may have been a factor in the mechanics which caused the rupture. Up to now, however, reports of rupture of normal chordae tendineae which are attached to diseased, distorted or calcified valves have not been found, and one might take the attitude that this calcification was not a factor in the rupture in this case. Whether or not it was a factor, the unique condition existed of a rupture of several normal chordae tendineae attached to one cusp of the mitral valve with resulting incompetency of the mitral valve. This patient's heart

was unable to adjust itself to the lesion so that a satisfactory circulation could be reestablished. It is interesting to note that prolonged cardiac decompensation can result in pure dilatation of the heart without increase in weight suggesting hypertrophy.

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OBSERVATIONS ON THE DURATION OF THE PHASES OF DIASTOLE IN MAN*†

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RECENTLY, on the basis of pressure curves recorded by optical methods in the various chambers of the heart and in large vessels, Wiggers[1, 2] has shown that the diastole of the heart can be subdivided into a number of phases: (a) the period of *protodiastole*, during which the semilunar valves are closing; (b) the *isometric relaxation phase*, during which the heart is relaxing without change in its chamber volume, the valves being closed; (c) the period of *rapid inflow* following the opening of the A-V valves during which the relaxing heart fills rapidly from the auricles; (d) the period of *diastasis*, during which the ventricle fills more slowly; and finally, (e) the period of *auricular systole* in which the auricles contribute to the filling of the heart as it is activated. In his studies Wiggers[1, 2] was able to define the durations of these phases in dogs, and in his laboratory Burstein[3] was able to establish the durations in man. Aside from some scattered observations on auricular systole, there are no further data dealing with this subject. An attempt was made in the present investigation to determine the duration of these phases in man with normal and abnormal hearts. It was felt that such a study might contribute to an evaluation of the disturbances in dynamics which various types of heart disease might cause. In man it is difficult to arrive at the nature of the filling process in any other way. It was thought that a correlation of such measurements with the dynamic changes established by study in acute animal experiments might permit the transference of data derived from animal experiments more directly to man.

PROCEDURE

In the present study 15 normal subjects and 35 patients with various types of heart disease were studied. These patients with abnormal hearts were divided into the following groups: (a) those in which *mitral stenosis* was the predominant lesion and in which there was a sinus rhythm; (b) those in which *aortic regurgitation* was the predominant lesion and in which there was a sinus rhythm; (c) those in which

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there was a combination of these two lesions and a sinus rhythm; (d) those with *myocardial damage* and sinus rhythm but no definite valvular disease; and (e) those with *auricular fibrillation* regardless of other cardiac involvement. Two cases of Group b were shown to be uncomplicated aortic regurgitation at autopsy.

All the subjects were brought to the heart station and placed in a prone or semiprone position. Simultaneous subclavian arterial and venous pulse tracings were obtained, usually with Lead II of the electrocardiogram. In some cases heart sounds were also recorded. The records were taken on film, using Wiggers' modification of the Frank

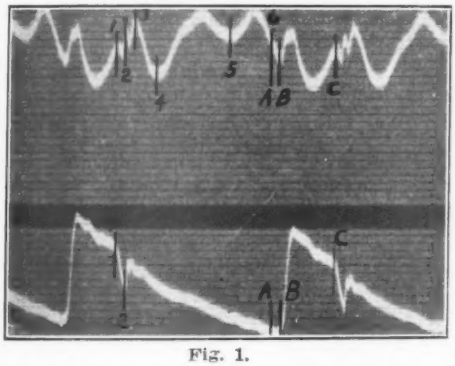

Fig. 1.

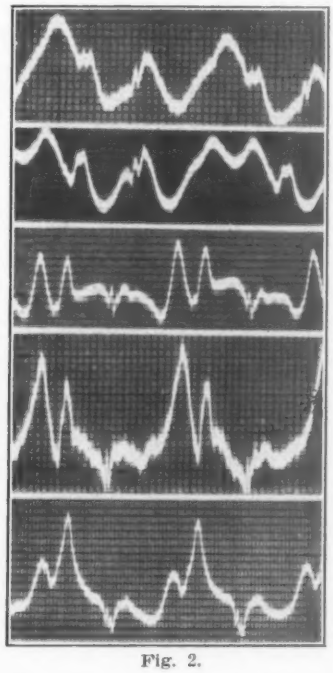

Fig. 2.

Fig. 1.—Simultaneous records of the pulses in the subclavian vein (upper) and artery (lower) showing the points used to define the different phases of systole and diastole. *A* to *B*, isometric contraction phase; *B* to *C*, systolic ejection phase; *1* to *2*, protodiastole; *2* to *3*, isometric relaxation phase; *3* to *4*, rapid inflow phase; *4* to *5*, diastasis; *5* to *6*, auricular systole.

Fig. 2.—Five samples of subclavian venous pulses showing some of its typical forms.

segment capsule[2] and the double-slit lamp of Katz and Baker,[4] with a point-o-lite bulb as a light source. Care was taken to avoid parallax (cf. Katz and Baker[4]). The patient held his breath while the record was taken in order to avoid distortion which might be produced by movement of the neck accompanying breathing. The other precautions utilized by Wiggers[2] were followed in taking these records. No attempt was made to quantitate the amplitude of the deflection which depends in these records on the degree of pressure applied on the

tambour, on the sensitivity of the recording system, on the proximity of the blood vessels to the tambour and on other factors. This inability to quantitate the amplitude did not interfere with the measurements of phasic durations. The procedure used in measuring the durations was similar to that established by Wiggers and employed by Burstein; it is shown in Fig. 1. It will be seen that the diastolic phases are measured primarily from the venous pulse and therefore give the duration of events in the right heart, the only exceptions being: (1) that protodiastole which is determined by the subclavian arterial pulse is a left-sided event; and (2) that the beginning of ventricular systole, and therefore the end of auricular systole, is determined by the left ventricle. Since Katz[5] has shown that the beginning and end of systole are not synchronous in the two ventricles, an unavoidable error is introduced in the determination of the phases of auricular systole and isometric relaxation of the right heart. The durations of the systolic phases which are measured from the arterial pulse are those of the left ventricle. We have found, in agreement with Wiggers,[2] that the contour of the subclavian venous pulse is variable, particularly in the variations introduced by the "systolic impact wave." In Fig. 2 are shown a few examples of the variability in contour encountered. With a little practice, however, and by correlating the venous pulse with the arterial pulse, no difficulty is encountered in defining the various diastolic phases. Only those records were used in this study in which the various phases could be clearly identified. The measurements could be made with an error of ± 0.01 sec.

RESULTS

A total of approximately 1,750 heart cycles were analyzed, using from 8 to 50 beats in each patient. The data thus obtained were handled in two ways: In the first place, the possible effect of cycle length on the different phases of diastole in the various types of cases studied was determined by charting the phase/cycle ratio as shown in Fig. 3, in which the ordinates give the duration of the phases in seconds and the abscissae the duration of the cycle length in seconds for each group of cases. In this way the effect of the lesion itself could be distinguished from the effect of cycle length. In order correctly to correlate the duration of these phases with the length of the heart cycle, the latter was measured from the beginning of one incisura to the next. This, the work of Wiggers and Katz has shown, is the proper way of analyzing the effect of heart rate on the phases of the cardiac cycle.

In the second place, a summary table, Table I, was made showing the extreme and predominant ranges and the commonest duration of each of these phases in the various types of heart diseases. To facilitate comparisons the measurements in the range of cycle length of

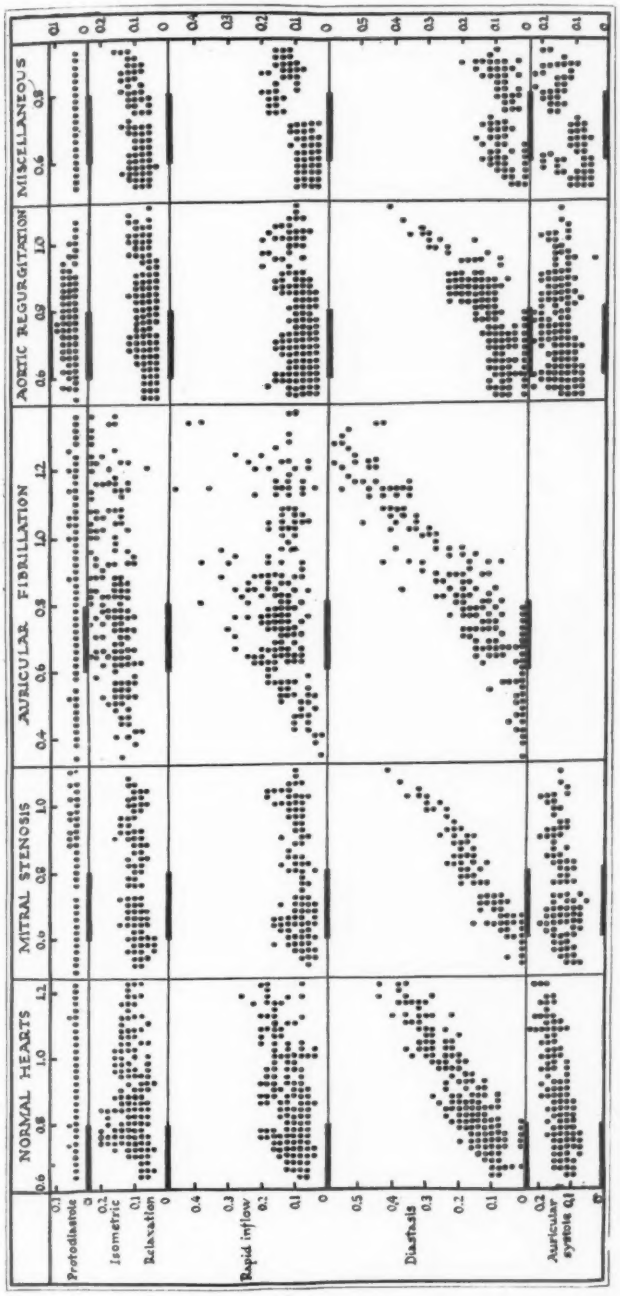

Fig. 3.—The dots represent the phase-cycle relationship in the individual pulse beats measured. These are assembled in groups, viz., the normal hearts, mitral stenosis, auricular fibrillation, aortic regurgitation, and miscellaneous. (See the classification in text.) The abscissae give cycle length in seconds—the ordinates, phase durations in seconds. For comparison the cycle length of from 0.6 to 0.8 of a second is blocked out on the lines separating the various phases in each group of cases.

from 0.7 to 0.8 second were selected, and the duration of the various phases in this cycle length range assembled in another summary table, Table II. A similar comparison can be made in Fig. 3 where cycle lengths from 0.6 to 0.8 second are indicated by blocks on the hori-

TABLE 1

		NORMAL HEARTS	PATHOLOGICAL HEARTS					
			MITRAL STENOSIS	AURICULAR FIBRILLATION	AORTIC REGURGITATION			MISCELLANEOUS
					COMPLICATED BY MITRAL LESION		UNCOMPLICATED	
					OF MODERATE DEGREE	OF ADVANCED DEGREE		
No. of cycles estimated		386	333	355	215	222	42	192
No. of individuals		15	9	6	6	4	2	8
DIASTOLIC PHASES		SECONDS	SECONDS	SECONDS	SECONDS	SECONDS	SECONDS	SECONDS
Protodiastole	Complete range	0.04-0.06	0.04-0.06	0.04-0.06	0.04-0.06	0.04-0.08	0.04-0.10	0.04
	Predominant range	0.04	0.04	0.04	0.04	0.06-0.08	0.04-0.08	0.04
	Commonest duration	0.04	0.04	0.04	0.04	0.06	0.04	0.04
Isometric	Complete range	0.04-0.20	0.04-0.16	0.06-0.30	0.04-0.12	0.04-0.10	0.04-0.12	0.04-0.16
Relaxation	Predominant range	0.08-0.14	0.08-0.12	0.12-0.16	0.06-0.10	0.04-0.08	0.08-0.10	0.08-0.12
	Commonest duration	0.08-0.12	0.08-0.12	0.12-0.16	0.06-0.08	0.04-0.08	0.10	0.08-0.12
Rapid Inflow	Complete range	0.04-0.26	0.04-0.18	0.00-0.46	0.04-0.18	0.04-020	0.04-0.14	0.04-0.20
	Predominant range	0.08-0.16	0.08-0.10	0.12-0.16	0.06-0.12	0.06-0.12	0.08-0.10	0.06-0.10
	Commonest duration	0.08-0.16	0.08	0.12-0.16	0.08-0.10	0.08-0.10	0.08	0.08-0.10
Diastasis	Complete range	0.00-0.44	0.00-0.42	0.00-1.38	0.00-0.42	0.00-0.24	0.00-0.08	0.00-0.20
	Predominant range	0.08-0.28	0.00-0.22	0.00-0.20	0.08-0.24	0.08-0.16	0.00-0.08	0.08-0.12
	Commonest duration	0.08-0.24	0.08-0.20	0.00-0.20	0.08-0.16	0.08-0.16	0.00-0.08	0.08-0.10
Auricular	Complete range	0.08-0.24	0.06-0.20		0.08-0.20	0.08-0.22	0.12-0.22	0.06-0.24
Systole	Predominant range	0.12-0.18	0.12-0.16		0.12-0.14	0.12.0.18	0.14-0.16	0.08-0.16
	Commonest duration	0.12-0.16	0.12-0.16		0.12-0.14	0.12-0.16	0.14-0 16	0.10-0.16

TABLE I—CONT'D

		NORMAL HEARTS	PATHOLOGICAL HEARTS					
			MITRAL STENOSIS	AURICULAR FIBRILLATION	AORTIC REGURGITATION			MISCELLANEOUS
					COMPLICATED BY MITRAL LESION		UNCOMPLICATED	
					OF MODERATE DEGREE	OF ADVANCED DEGREE		
No. of cycles estimated		386	333	355	215	222	42	192
No. of individuals		15	9	6	6	4	2	8
SYSTOLIC PHASES		SECONDS	SECONDS	SECONDS	SECONDS	SECONDS	SECONDS	SECONDS
Isometric Contraction	Complete range	0.04-0.06	0.02-0.06	0.04-0.10	0.04-0.08	0.04-0.08	0.04-0.10	0.02-0.10
	Predominant range	0.04	0.04	0.04-0.08	0.04	0.04-0.06	0.04-0.08	0.04-0.08
	Commonest duration	0.04	0.04	0.04-0.08	0.04	0.04-0.06	0.04-0.08	0.04
Systolic Ejection	Complete range	0.20-0.34	0.16-0.30	0.08-0.32	0.16-0.30	0.14-0.34	0.18-0.28	0.16-0.36
	Predominant range	0.24-0.28	0.18-0.26	0.18-0.24	0.18-0.28	0.24-0.28	0.22-0.24	0.20-0.28
	Commonest duration	0.26	0.18-0.26	0.22-0.24	0.26-0.30	0.24-0.28	0.22-0.24	0.20
TOTAL DIASTOLE								
	Complete range	0.38-0.90	0.26-0.74	0.18-1.74	0.32-0.74	0.32-0.62	0.36-0.46	0.28-0.62
	Predominant range	0.44-0.56	0.32-0.48	0.26-0.64	0.38-0.56	0.48-0.56	0.38-0.44	0.40-0.56
	Commonest duration	0.48-0.52	0.44	0.28-0.40	0.52-0.56	0.52	0.40	0.52
TOTAL SYSTOLE								
	Complete range	0.24-0.38	0.20-0.36	0.16-0.40	0.20-0.36	0.20-0.42	0.26-0.36	0.20-0.38
	Predominant range	0.28-0.32	0.24-0.28	0.20-0.32	0.30-0.34	0.28-0.32	0.26-0.30	0.24-0.32
	Commonest duration	0.30-0.32	0.24-0.28	0.24-0.32	0.30-0.34	0.32	0.30	0.24-0.26
TOTAL CYCLE								
	Complete range	0.64-1.22	0.48-1.06	0.34-2.06	0.54-1.06	0.56-1.00	0.64-0.76	0.52-0.92
	Predominant range	0.72-0.82	0.64-0.72	0.52-0.88	0.84-0.92	0.80-0.88	0.70-0.74	0.70-0.86
	Commonest duration	0.76	0.64	0.52-0.88	0.88	0.84-0.88	0.70	0.70

Table II

Duration of Phases of Cardiac Cycle When Cycle Length Is 0.70 to 0.80 Second in Duration

		Normal Hearts	Pathological Hearts					
			Mitral Stenosis	Auricular Fibrillation	Aortic Regurgitation			Miscellaneous
					Complicated by Mitral Lesion		Uncomplicated	
					of Moderate Degree	of Advanced Degree		
Diastolic Phases		Seconds	Seconds	Seconds	Seconds	Seconds	Seconds	Seconds
Protodiastole	Predominant range	0.04-0.06	0.04	0.04	0.04-0.06	0.04-0.08	0.04-0.10	0.04
	Commonest duration	0.04	0.04	0.04	0.04-0.06	0.06	0.06-0.08	0.04
Isometric Relaxation	Predominant range	0.04-0.20	0.08-0.12	0.10-0.22	0.08-0.10	0.04-0.08	0.04-0.12	0.06-0.12
	Commonest duration	0.08-0.16	0.10	0.14-0.16	0.10	0.06	0.08-0.10	0.06-0.12
Rapid Inflow	Predominant range	0.04-0.20	0.04-0.14	0.08-0.38	0.06-0.16	0.04-0.14	0.04-0.14	0.04-0.18
	Commonest duration	0.06-0.12	0.06-0.08	0.12-0.20	0.06-0.12	0.06-0.10	0.04-0.08	0.06-0.16
Diastasis	Predominant range	0.00-0.22	0.00-0.20	0.00-0.24	0.00-0.16	0.00-0.16	0.00-0.08	0.04-0.10
	Commonest duration	0.08-0.20	0.12-0.20	0.16-0.20	0.08-0.10	0.08-0.12	0.04-0.08	0.06-0.08
Auricular Systole	Predominant range	0.08-0.18	0.06-0.16		0.10-0.14	0.12-0.22	0.12-0.22	0.08-0.20
	Commonest duration	0.12-0.16	0.12-0.16		0.12	0.12-0.20	0.14-0.20	0.10-0.18
Systolic Phases								
Isometric Contraction	Predominant range	0.04-0.06	0.04	0.04-0.08	0.04	0.04-0.08	0.04-0.10	0.04-0.06
	Commonest duration	0.04	0.04	0.04-0.08	0.04	0.04-0.04	0.08	0.04
Systolic Ejection	Predominant range	0.20-0.28	0.22-0.26	0.14-0.24	0.24-0.28	0.20-0.28	0.18-0.28	0.16-0.28
	Commonest duration	0.22-0.26	0.22-0.26	0.18-0.20	0.26-0.28	0.22-0.28	0.22-0.28	0.18-0.24
Total Diastole								
	Predominant range	0.40-0.54	0.42-0.52	0.44-0.56	0.40-0.52	0.40-0.52	0.36-0.46	0.40-0.56
	Commonest duration	0.44-0.52	0.42-0.48	0.46-0.54	0.40-0.52	0.44-0.48	0.40-0.44	0.42-0.54
Total Systole								
	Predominant range	0.24-0.32	0.22-0.30	0.22-0.28	0.28-0.32	0.24-0.38	0.26-0.36	0.24-0.32
	Commonest duration	0.26-0.30	0 24-0.28	0.22-0 28	0.28-0.30	0.28-0.32	0.28-0.32	0.24-0.28

zontal lines separating the different phases in each group of cases.

A comparison was also made of the relation of the durations of the entire ventricular systole and the entire diastole to cycle length in each type of case. The results are assembled in Fig. 4, in which the lines represent means of the plotted points in each type of case represented.

DISCUSSION

An analysis of these tables and charts led us to the following summary of results:

Protodiastole was remarkably constant in duration and did not vary with cycle length. It was within the normal limits in most of the pathological conditions encountered. However, the cases with aortic

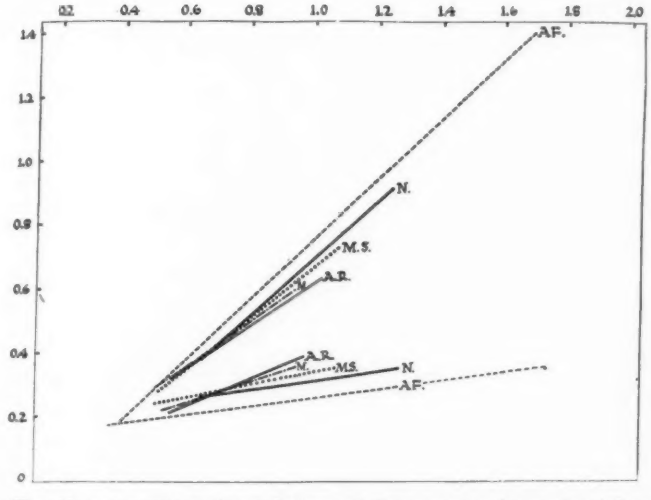

Fig. 4.—The lines represent the relation of the mean values of total ventricular systole (lower curves) and total ventricular diastole (upper curves) to cycle length. Abscissae represent cycle length in seconds—ordinates, the duration of systole and diastole in seconds. *N* is the mean of the group of normal hearts; *M.S.*, that of the group with mitral stenosis; *A.R.*, the group with aortic regurgitation; *A.F.*, the group with auricular fibrillation; and *M*, the miscellaneous group. (See the classification in text.)

regurgitation, uncomplicated or complicated, showed a conspicuous lengthening of this phase.

The isometric relaxation phase was not greatly influenced by cycle length. The variation in the duration of this phase was greater than normal in cases of auricular fibrillation, a variation which was apparently not dependent upon cycle length. It was consistently shortened in cases of aortic regurgitation.

The rapid inflow phase did not vary with cycle length. Its duration was relatively shorter than normal in all the pathological types of cases except in auricular fibrillation. In auricular fibrillation the scatter of individual determinations was more marked than in normal cases.

Diastasis was the one phase which varied directly with cycle length in every group of cases. This is brought out most clearly in the group of cases of auricular fibrillation where the greatest variation in cycle length was encountered. Some of these patients were digitalized, which may account for the extremely long diastolic phases found. However, the scatter was greater in auricular fibrillation than in the normals. In the other types of pathological cases the duration of diastasis was relatively shorter than normal.

Auricular systole showed no variation with cycle length. It tended to be longer than normal in the aortic regurgitation cases. Obviously, this phase was absent in cases of auricular fibrillation.

As had been already established by previous workers, both the total systole and the total diastole vary with the cycle length, the former showing less change than the latter. Except for auricular fibrillation it was found that the duration of systole was longer and the duration of diastole shorter in the abnormal cases than in the normal at the same cycle lengths. The auricular fibrillation cases, however, in confirmation of the observations of Katz and Feil,[7] showed a total systole shorter than normal and a lengthened total diastole (longer than normal at the same cycle length).

TABLE III

COMPARATIVE TABLE OF PHASE DURATIONS IN NORMAL HEARTS

		OUR FINDINGS 15 CASES 386 CYCLES	FINDINGS OF WIGGERS AND ASSOCIATES
DIASTOLIC PHASES		SECONDS	(BURSTEIN) SECONDS
Protodiastole	Complete range	0.04-0.06	0.016-0.060
	Predominant range	0.04	0.030-0.050
	Commonest duration	0.04	0.038
Isometric Relaxation	Complete range	0.04-0.20	0.037-0.130
	Predominant range	0.08-0.14	0.060-0.090
	Commonest duration	0.08-0.12	0.076
Rapid Inflow	Complete range	0.04-0.26	0.055-0.173
	Predominant range	0.08-0.16	0.090-0.130
	Commonest duration	0.08-0.16	0.113
Diastasis	Complete range	0.00-0.44	0.080-0.708
	Predominant range	0.08-0.28	(Wiggers)
	Commonest duration	0.08-0.24	0.163
Auricular Systole	Complete range	0.08-0.24	
	Predominant range	0.12-0.18	(Wiggers)
	Commonest duration	0.12-0.16	0.110

In general our findings on the duration of the diastolic phases in normal cases agree fairly well with those given by Wiggers and by Burstein for man, as the comparison summarized in Table III will show. They, however, have reported averages, while we have reported the range of commonest durations; hence our durations for the various phases tend to be somewhat longer than those they give.

Definite changes in the duration of the diastolic phases were found only in the cases of aortic regurgitation and the cases of auricular fibrillation. A prolongation of total systole and abbreviation of diastasis were found in all types of abnormal hearts studied except in auricular fibrillation. The results confirm previous work since a prolongation of systole has been experimentally produced in mitral stenosis by Katz and Siegel[8] and in aortic insufficiency by Wiggers.[9] Clinically, Feil and Forward[10] have reported on mitral stenosis and Katz and Feil[11] on aortic insufficiency. An abbreviation in total systole such as that reported by Feil and Katz[12] in patients with heart failure was not encountered in this study, as none of these patients had advanced cardiac failure.

Confirming the impression of Katz and Feil[7] that the synergically contracting auricles in man contribute a definite quantity of blood to the ventricles, a definite abbreviation of total systole was found in auricular fibrillation. In auricular fibrillation it was found that except for protodiastole all the diastolic phases, namely, isometric relaxation, rapid inflow and diastasis, were prolonged for a given cycle length. This may in part be due to the digitalis which was used in some of these patients. The longer durations of the rapid inflow phase might be viewed as an attempt to compensate for the absence of the auricular contribution.

The definite lengthening of protodiastole found in aortic insufficiency is also shown in the curves published by Wiggers and Maltby[13] following experimentally produced aortic insufficiency. It indicates that the time for closure of the semilunar valves is prolonged in aortic insufficiency. The decided shortening in the isometric contraction period in aortic insufficiency may be due to an error in establishing the onset of this phase which would result if the prolongation of ventricular systole in the left ventricle were greater than that in the right. As pointed out above, the protodiastole as determined is that of the left ventricle, while isometric relaxation is that of the right ventricle. An asynchronism of the end of protodiastole would therefore mask the true beginning of isometric relaxation and cause an apparent (but not necessarily real) abbreviation of this phase. It is difficult to explain, otherwise, why the isometric relaxation period of the right ventricle should be abbreviated. The lack of abbreviation in the isometric relaxation phase in the other abnormal hearts studied would, on this basis, be interpreted as indicating a parallel prolongation above normal in the systole of both ventricles.

These observations show that, in the absence of advanced heart failure, the dynamics of filling the right ventricle are not appreciably altered—except for the shortening of the period of diastasis—unless auricular fibrillation is present. Studies are in progress to see if this is also true in patients with advanced heart failure.

SUMMARY

We have measured the duration of each of the separate phases in approximately 1,750 cardiac cycles in 50 subjects, 15 of whom had normal hearts, the remaining 35 having some type of cardiac lesion. The diastolic phase durations in these different types of lesion have been tabulated and analyzed. These findings may be summarized as follows:

1. In auricular fibrillation total systole was found to be definitely shorter and total diastole definitely longer than in normal cases at the same cycle lengths. In all the other pathological types total systole was longer and total diastole shorter than in normal cases at the same cycle lengths.

2. In digitalized cases of auricular fibrillation the isometric relaxation and the rapid inflow phases tended to be prolonged.

3. In aortic regurgitation, protodiastole tended to be prolonged, isometric relaxation to be shortened, and auricular systole to be slightly prolonged in comparison to the duration of these phases in normal hearts.

We are grateful to Dr. Louis N. Katz at whose suggestion and under whose guidance this research was undertaken, for his advice and criticism.

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THE PRECORDIAL LEAD IN 104 NORMAL ADULTS*

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THE use of the precordial† ("chest" or "fourth") lead in the diagnosis of heart disease is rapidly increasing. Before clinical application of the precordial lead readings can be of value, it is necessary to have tracings of normal people as controls. Katz and Kissin[1] have published the measurements from records of 25 individuals, but a larger number is necessary before importance can be attached to the findings. These investigators placed their patients on the left side when taking the chest lead, but there is an objection to this procedure, as such a movement may shift and rotate the heart and hence change the electrocardiographic picture.

The 104 individuals whose records are reported in this paper were carefully examined at Cornell University Medical College in the years 1926, 27, 28. At that time the three standard leads of the electrocardiogram, and also anteroposterior and transverse chest leads were taken. Everything possible was done to make certain that the individuals were normal. They had no complaints; physical examination was negative; blood pressure tests, urine examinations, teleroentgenograms, electrocardiograms, exercise tolerance tests were all normal.

The series consisted of 26 women ranging in age from twenty-eight to sixty-five years, the average age being forty years, and 78 men from twenty-seven to seventy-four years old, the average age being forty-four years. In other words, it was a series comprised of normal adults.

The anterior electrode was placed near the lower end of the sternum, about the level of the apex of the heart and slightly to the left of the midline. The form of the electrocardiogram changed very little when this electrode was moved from the middle of the sternum to the region of the apex but not beyond. The posterior electrode was located on the back over the vertebral column at about the same level as the anterior or slightly higher. To the anterior electrode the wire from the right arm terminal of the galvanometer and to the posterior electrode the wire from the left arm terminal of the galvanometer were attached.

*From the Department of Medicine, Cornell University Medical College.

†The expression "precordial" lead is used in this paper synonymously with chest or fourth or anteroposterior lead.

TABLE I

	HEART RATE	SIZE P-WAVE	DURATION P-WAVE	P-Q	SIZE Q	SIZE R	DURATION Q-R	SIZE T	DURATION T	TRANSITION R-T	DURATION R-T*
Average	77	−0.74 mm.	0.06 sec.	0.15 sec.	− 5.3 mm.	+10.7 mm.	0.09 sec.	−3.3 mm.	0.19 sec.	−1.0 mm.	0.26 sec.
Range of 80% cases	60 to	−0.5 to	0.04 to	0.12 to	− 3.0 to	+ 5.0 to	0.08 to	−1.5 to	0.16 to	−1.0	0.24 to
	85	−1.0	0.08	0.16	− 7.0	+14.0	0.09	−4.0	0.24		0.28
Low	50	−1.5	0.0	0.10	− 1.5	+ 2.5	0.08	−1.0	0.08	0.0	0.20
High	100	0.0	0.10	0.18	−14.0	+17.5	0.10	−7.5	0.26	−2.0	0.32
Exceptional readings†	120	−2.0		0.20		+19.0	0.06				
		+0.5				+23.0					
		+2.0				+26.0	0.12	+0.5			

*Measured from end of R through to end of T-wave.
†Each figure is obtained from the precordial lead of a single patient.

CHARACTERISTICS OF THE NORMAL PRECORDIAL LEAD

The P-wave was inverted; the amplitude averaged –0.7 mm. The average duration of the P-wave was 0.06 second. The limits are given in Table I where the measurements are summarized. At first glance, the P-wave (Fig. 1) appeared diphasic, for the interval between the P-wave and the QRS group was always slightly above the isoelectric level. This was due to the end deflection of the auricular contrac-

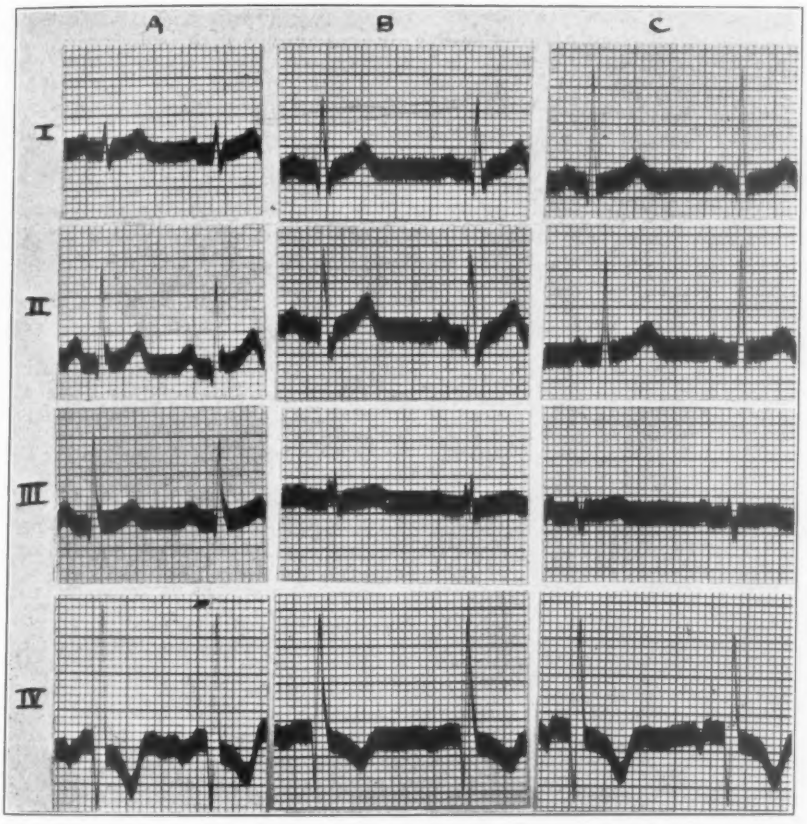

Fig. 1.—*A, B, C,* Three normal individuals with Leads I, II, III and precordial (chest or fourth) lead.

tion, the "T-wave of the P-wave," so to speak. In the standard electrocardiogram this end deflection of the P-wave is usually evident but is not so large as in the precordial lead.

The auriculoventricular conduction time, that is, the P-Q interval, measured 0.15 second, but the range was from 0.10 to 0.18 second. It attained 0.20 second once.

The QR group is perhaps a better term than the QRS group, for in the precordial lead there were only two waves visible. In the ordinary standard electrocardiogram three waves are common, and one

wave alone is not uncommon. In our series, the first wave of the QR group was always a downward deflection, or Q-wave. The absence of a Q-wave, therefore, is abnormal. The average size was –5.3 mm., but the amplitude ranged from –1.5 to –14.0 mm. Not one Q-wave measured less than –1.5 mm.

The next wave, the R-wave, was upright. Its average height was +10.7 mm., ranging usually from +2.0 to +17.0 mm., but attaining +19.0 mm., +23.0 mm., and +26.0 mm., each, once. The Q-wave was usually smaller than the R-wave, but to this there were eleven exceptions. The absence of an R-wave or one whose size is less than +2.0 mm. is abnormal.

The duration of the QRS was 0.09 second. In fact, the variation shown in this group was apparently much less than that in the standard electrocardiogram. It ranged, nevertheless, from 0.06 second to 0.12 second, each of these limits being attained only once, so that one is safe in stating that the upper limit of normal is 0.10 second. Notching or slurring was never present in the precordial chest lead of the normal individual. On the other hand, this is not uncommon in Lead III of the standard tracing.

The R-T transition of the precordial electrocardiogram differed from the RS-T transition of the standard record. The T-wave was angularly inverted almost immediately after the R-wave, with hardly a semblance of isoelectric level (Fig. 1). The average of the R-T transition was 0.08 second. The R-T interval, measured from the end of the downstroke of the R-wave to the end of the T-wave, was 0.26 second, but the range was from 0.20 to 0.32 second. The R-T transition usually was 1 mm. below the isoelectric level; it was isoelectric on eight occasions, but never once above the isoelectric line.

The T-wave was inverted. The negativity ranged in amplitude from –1.0 mm. to –6.0 mm. Once indeed it measured –7.5 mm. Any T-wave greater than –6.0 mm. is probably abnormal.

The average duration of the T-wave was 0.19 second, but there were wide variations, i.e., from 0.08 second to 0.26 second.

There were a few exceptions to the foregoing descriptions. The P-wave was positive in 2 instances out of the 104 examinations. This occurred in subjects of forty-eight and thirty years of age, respectively. These individuals were considered normal in every respect, but they had long, narrow hearts. It may be that an unusual rotation of the heart was responsible for these variations from the predominant findings.

The T-wave was barely positive once, about +0.5 mm. This was present in a woman forty-four years old in whom history, physical examination, teleroentgenogram of the heart and laboratory examinations were normal. Her electrocardiogram revealed a normal sinus rhythm with a left ventricular preponderance. The only doubtful

finding was an inverted cove plane T-wave in Lead III. The patient was reexamined in January, 1934. All examinations including fluoroscopy of the heart and lung were negative, but the precordial lead now revealed not only a positive T-wave of +0.5 mm., but a notched QR and an R preceding the Q-wave, an observation which is considered definitely abnormal and which was never found in any of the first 104 records. For these reasons it is my opinion that the inverted T-wave in Lead III was an abnormal finding, and that the patient did not possess a normal heart. Moreover, the fact that the slightly positive T-wave of the precordial lead was the only exception in the 104 cases proves that it may be discarded from a statistical point of view. In other words, a positive T-wave in the precordial lead should always be considered abnormal.

It appears from the foregoing that the precordial lead may help to decide when an inverted T-wave in the third lead of the electrocardiogram is of significance.

Left ventricular preponderance on the electrocardiogram occurred 44 times. The precordial tracings in these cases showed nothing different from those observed in the remaining cases.

COMMENT

Many types of electrodes were experimented with in taking chest leads. One of the simplest of these was an ordinary glass funnel, with outside diameter of about from 1.5 to 2 inches. Inside the funnel, as near the periphery as possible, were wound a few coils of thick copper wire which emerged through the narrow end. The funnel was stuffed with a wad of absorbent cotton moistened with warm salt water. The cotton was bulky so that it formed the area of contact with the chest wall. The glass, held in the hand, served as an insulator. Another such electrode was held in place posteriorly. I am now substituting the posterior chest electrode with the left leg electrode. As Wilson[2] has shown, the lead over the heart is the important one, and the other lead may be placed at a greater distance from the heart without significant changes in the electrocardiogram. I have confirmed this observation in at least 30 patients, and hence use the funnel electrode over the precordium, and the left leg as the indifferent electrode. The precordial lead is then taken as one ordinarily derives the standard Lead II. This method is simpler than utilizing both the anterior and posterior chest electrodes.

It was usually found unnecessary to rub the skin at the site upon which the funnel was placed, unless the chest was hairy. The best means of reducing resistance was by making two or three very superficial scratches with a hypodermic needle. It was never necessary to draw blood.

It will be observed that the P- and T-waves were inverted, and on this account many writers have suggested that the chest leads should be reversed. The P-wave would then be upright, the first wave of the QRS group would be upright, the second inverted, and the T-wave would be positive. In the standard electrocardiogram the waves usually occur in this form; hence the advantage of reversing the leads. The measurements given in Table I would still hold except that their signs would change.

SUMMARY

For the precordial lead the right arm electrode is placed on the anterior chest, just to the left of the sternum about the level of the apex, and the second electrode is on the left leg. The record is then taken as one usually derives Lead II of the standard electrocardiogram. This method is simpler than that of placing one electrode on the front and the other on the back of the chest.

A simple glass electrode is described for obtaining precordial leads.

It is suggested that the electrodes of the precordial lead be reversed so that P, R and T will be positive and only S inverted, just as they are in the standard electrocardiogram of normal adults.

The precordial chest lead in 104 normal individuals is summarized. In this series the P-wave is shown to be negative, is not more than –1.5 mm. and is usually followed by an end deflection above the isoelectric level. The P-Q interval averages 0.15 second. The QRS group is always diphasic, and never notched or slurred. Its duration is 0.09 second. The absence of the Q-wave or of the R-wave is definitely abnormal. The Q-wave averages –5.3 mm. in size and the R-wave, +10.7 mm. No Q-wave less than –1.5 mm. and no R-wave less than +2.5 mm. in size was ever observed. The R-T transition is below the isoelectric level, occasionally just isoelectric. A positive R-T transition or one that is more than 2 mm. below the isoelectric is definitely abnormal. The T-waves are always inverted and usually are less than –6.0 mm. in size.

The precordial lead may prove of service in interpreting which T-wave inversions of the third lead are abnormal.

Left ventricular preponderance in the standard electrocardiogram of normal adults does not change the form of the precordial lead.

My thanks are due to Dr. Harold E. B. Pardee for his many helpful suggestions.

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THE EFFECT OF CONDENSERS IN THE ELECTROCARDIOGRAPH*†

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THE taking of an electrocardiogram has certain commonly appreciated inconveniences. Compensation and current reversal are necessary; the string often tends to move off the field, and a well-trained operator is required. These difficulties are largely obviated by the use of a condenser (capacitance) in the electrocardiographic circuit, since the string then returns toward the center of the field automatically without the use of a compensating current. In fact, most of the amplifier type instruments available today make use of condensers.

A condenser placed in series with the patient and the electrocardiograph will suppress the low frequencies primarily due to "skin current" but will permit the passage of the cardiac current. A capacitance represents an impedance to the flow of electric current inversely proportional to the frequency of alternation of the current. It offers a practically infinite impedance to low frequency currents which are evidenced by a drift ("skin current"), whereas it offers little impedance to currents caused by the rapidly fluctuating heart voltage.

The use of the condenser has been mentioned before. Cremer[1] first reported its use for recording nerve currents. Later[2] he reported the possibility of its use in electrocardiography. Kraus and Nicolai[3] mentioned the condenser as a means of automatic compensation, but on the basis of work done up to that time did not recommend its use because of the distortion introduced. Zwicke[4] as well as Rothberger and Winterberg[5] discussed the effect of the condenser qualitatively and showed that the magnitude of the distortion depends not only on the size of the condenser, but also on the value of the resistance of the circuit. Kahn[6] and Weber[7] noted the condenser as a method of compensation, and like Kraus and Nicolai[3] did not advise its routine use because of distortion. Schellong[8] presented tracings to illustrate the distortion introduced by condensers and showed that the effect of polarization is similar to that of capacitance. Lueg[9] showed that the introduction of condensers (of small capacity—7 microfarads, 2 microfarads, and 0.5 microfarads capacity) into the string galvanometer circuit will cause flattening of the waves so that the records resemble those of myxedematous individuals.

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Dock[10] demonstrated the effect of condensers in the string galvanometer circuit, as well as the effect of capacitance in the amplifier type of electrocardiograph. He questioned the accuracy of records obtained with the amplifier type of instrument having condensers in the circuit. Ernstene and Levine[11] compared records taken with the amplifier type of electrocardiograph (circuit constants not given) with those taken with the string galvanometer. They found slight differences in the amplitude of the deflections of the two kinds of records, but considered amplifier records satisfactory. Pardee[12] expressed surprise at Dock's criticism[10] (on the score of condensers) of the amplifier instrument. He made comparative records with both types of instruments and concluded that amplifier records do not show distortion and that high external ("skin") resistance will cause distortion in string galvanometer tracings, but not in amplifier records. Because of the predominantly qualitative trend of all the available data, a more thorough study from the quantitative point of view seemed desirable.

In the electrocardiograph there are two important sources of distortion. One is the distortion due to the imperfect mechanical properties of the recording system. The other is due to the imperfect electrical properties of the circuit. For electrocardiography, where very high frequencies (over 1,000 per second) need not be considered, these two types of distortion may be very simply differentiated in their effect on the record. The former, primarily due to the inertia of the moving system, is almost exclusively responsible for any loss of higher frequencies, because of the inability to follow very rapid fluctuations with fidelity.[13] The latter, in all practical systems heretofore described, due to capacitance in the electrical circuit, is responsible for losses at low frequencies, resulting in a distortion, the details of which are the subject of this study.

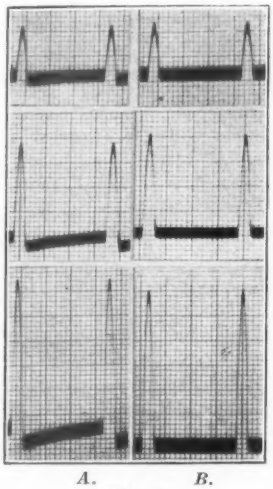
METHOD

In order to investigate the distortion experimentally it appeared desirable to dispense with the use of patients as sources of voltage, since in an actual electrocardiogram slight variations in the waves occur from cycle to cycle. An artificial source which could be depended upon for exact duplication, with electrical properties similar to that of a patient, offers great advantages. Such a device was constructed. It consists essentially of a gas-filled photoelectric cell and a light source between which, with a suitable optical system, a disc is rotated by a spring motor. The disc is notched to correspond to the desired voltage waves. As it turns it occludes more or less light from the cell, thus causing more or less current to flow in the photo-cell circuit. A shunt in the circuit acts as the patient. The photo-cell current is high enough to permit the application of the voltage across

the shunt, the resistance of which may be made as low as 1,000 ohms, directly to the electrocardiograph without the interposition of amplifiers or other possible sources of distortion. With this device any recurring wave form may be produced at will by cutting the proper disc.

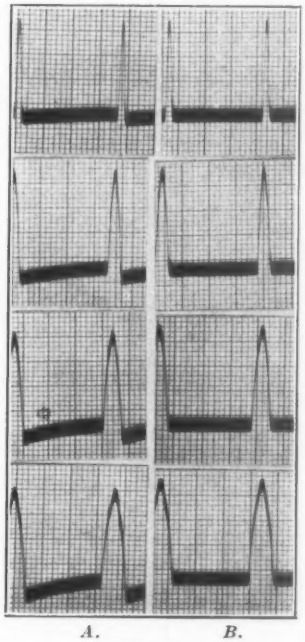
FACTORS DETERMINING THE MAGNITUDE OF THE DISTORTION

The simple circuit, consisting of galvonometer, condenser, and patient in series, is the basis for consideration. If at the beginning of a wave, say the R-wave, the condenser is uncharged, at the end of the wave it will be left with a charge. This charge on the condenser causes a deflection of the galvanometer opposite in direction to the wave



A. *B.*

Fig. 1.



A. *B.*

Fig. 2.

Fig. 1.—Effect of amplitude of the wave on the distortion: *A*, with condenser; *B*, without condenser.

Fig. 2.—Effect of duration of the wave on the distortion: *A*, with condenser; *B*, without condenser.

just terminated. The effect of the condenser is therefore to produce an overshooting of the end of the wave. In addition, during the course of the wave the condenser is accumulating the charge so that the amplitude of the wave will be reduced.

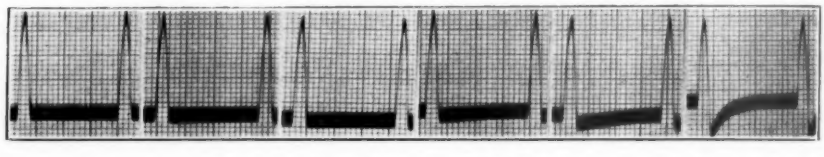
The actual extent of these distortions, that is the magnitude of the overshooting and the reduction in amplitude, depends upon the size of the wave being recorded and the constants of the circuit.

The distortion is proportional to the amplitude of the wave. This is illustrated in Fig. 1, which shows waves of 1, 2, and 3 millivolts, all having the same duration, produced artificially by means of the photo-

sensitive device. Fig. 1 *A* shows the waves as recorded with a condenser in the circuit, while Fig. 1 *B* shows the same waves as recorded without a condenser.

The distortion is also proportional to the duration of the wave. Fig. 2 shows waves of 0.05, 0.1, 0.15, and 0.2 second duration, all having the same amplitude. Fig. 2 *A* shows the waves as recorded with a condenser in the circuit, while Fig. 2 *B* shows the same waves as recorded without a condenser.

The distortion is inversely proportional to the product of the capacity of the condenser in farads and the resistance of the entire circuit in ohms. Since this product is known as the time constant, we may say that the distortion is inversely proportional to the time constant. This is illustrated in Fig. 3, which shows a series of waves all of the same amplitude and duration, as recorded without a condenser in the circuit, and with various time constants; namely, 3, 2, 1, 0.5, and 0.1 seconds. The time constant may be increased either by increasing the resistance of the circuit or increasing the capacity of the condenser.



A. *B.* *C.* *D.* *E.* *F.*

Fig. 3.—Effect of time constant on the distortion: *A*, without condenser; *B*, $\tau = 3$ sec.; *C*, $\tau = 2$ sec.; *D*, $\tau = 1$ sec.; *E*, $\tau = 0.5$ sec.; *F*, $\tau = 0.1$ sec.

The reduction in amplitude follows the same laws and is in general about half as great as the overshooting. Figs. 1, 2, and 3 verify this point.

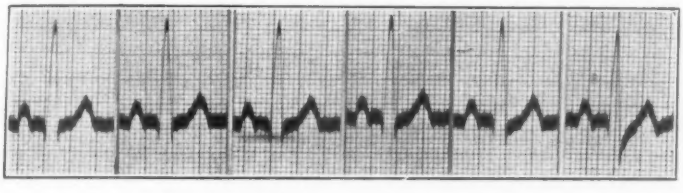
CALCULATION OF THE DISTORTION*

In order to utilize these results to best advantage it is desirable to be able to calculate from a recorded wave the distortion contained in it; that is, for example, how much of a recorded depression of an RS-T interval is real and how much is due to the use of a condenser. In that way it will be possible either to correct records taken with inadequate condensers or to determine how much capacity is necessary for clinically satisfactory recording.

The quantitative relationships are very readily found. The charge delivered to the condenser during the passage of a wave is equal to the average current flowing in the circuit multiplied by the duration of the wave. The average current flowing in the circuit is equal to the average voltage divided by the resistance. If the wave is considered

*The mathematical details of the derivation of the formulas and statements embodied in this paper will be furnished, upon request, by the authors to those interested.

to be triangular in shape, a fair assumption, the average voltage is one-half the amplitude of the wave. Hence, if R is the resistance of the circuit, H is the amplitude of a wave and T its duration, the charge delivered to the condenser during its passage will be given by $\frac{HT}{2R}$. This charge, as has been stated before, causes a deflection of the galvanometer because a charge on a condenser is always accompanied by a voltage difference equal to the charge divided by the capacity of the condenser. In this case, then, the deflection of the galvanometer after the passage of the wave, or the overshooting, will be given by $\frac{HT}{2RC}$. The quantity RC in this expression is the time constant and will be denoted by τ so that finally the overshooting is given by $\frac{HT}{2\tau}$.



A B C D E F

Fig. 4.—Artificial electrocardiograms with various time constants; agreement between calculated and measured values of the distortion: *A*, without condenser: RST depression 0.4 m.m., R amplitude 20; *B*, $\tau = 3$ sec. RST depression; Observed 0.5, Calculated 0.6, R amplitude: Observed 20, Calculated 19.9; *C*, $\tau = 2$ sec. RST depression: Observed 0.7, Calculated 0.7, R amplitude: Observed 20, Calculated 19.8; *D*, $\tau = 1$ sec. RST depression: Observed 1.1, Calculated 1.1, R amplitude: Observed 19.5, Calculated 19.6; *E*, $\tau = 0.5$ sec. RST depression: Observed 1.7, Calculated 1.9, R amplitude: Observed 19.5; Calculated 19.2; *F*, $\tau = 0.1$ sec. RST depression: Observed 6, Calculated 8.3, R amplitude: Observed 17, Calculated 16.

By a very similar argument it can be shown that the diminution of amplitude of the initial stroke of a wave is given by $\frac{Ht}{2\tau}$ where t is the duration of the initial stroke.

In order to simplify this discussion it has been assumed that at the beginning of the wave the condenser is uncharged. Actually, since any wave is merely one of a series of successive waves, this is not the case. If account is taken of the residual charge, the distortion calculated in accordance with the above formulas is, in an extreme case, in error by only 0.2 mm. for a time constant of one second and proportionately less for longer time constants. When all the waves are in the same direction, i.e., P, QRS and T, all erect or all inverted, the calculated distortion is slightly greater than the real distortion. When there are inverted waves, our formula may actually underestimate the distortions.

CLINICAL SIGNIFICANCE OF THE DISTORTION

Fig. 4 shows a series of artificial electrocardiographic curves taken with the help of the same photosensitive device mentioned above. It is readily seen that the most significant distortion from the clinical point of view is the depression of the RS-T segment due to the condensers. Inasmuch as attention is paid to the RS-T segment in the diagnosis of coronary artery disease, rheumatic fever, and other conditions, deviation of this segment assumes significance. Since the distortion is proportional to the size of the wave, small waves may show no distortion, while large waves will show appreciable distortion.

The time relationships, such as the PR interval, the width of the QRS straddle, the RR interval, remain unchanged with the use of condensers. This is readily verified in Fig. 4.

APPLICATION TO AMPLIFIER TYPE OF ELECTROCARDIOGRAPHS

This discussion applies directly only to the simple galvanometer circuit in which the patient, galvanometer, and condenser are in series.

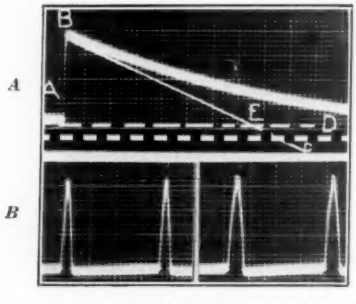


Fig. 5.—*A*, Determination of the effective time constant for an amplifier type electrocardiograph. *B*, Distortion introduced by this particular electrocardiograph.

The formulas may also be applied to amplifier type electrocardiographs in which condensers are used, if in place of τ, which for the simple circuit is the product of the capacity of the condenser in farads and the total resistance (galvanometer and patient) in ohms, is substituted the equivalent time constant.

The equivalent time constant may be determined by applying a potential of a few millivolts to the leads without a patient. The record obtained will show a sudden rise and then a gradual drop back to the isoelectric line. Fig. 5 *A* shows such a record. If the straight line *BC* is drawn tangent to the curve at the peak, the time between the initial rise and the intersection *E*, with the zero line, *AD*, measured in seconds, is the equivalent time constant, in this case 1.4 seconds.

Fig. 5 *B* shows the distortion introduced by the instrument, the time constant of which is derived in Fig. 5 *A*.

In the string galvanometer with condensers in the circuit, changes in the patient's resistance will affect the time constant, whereas in the amplifier instrument as generally constructed the time constant is independent of the patient's resistance.

OPTIMUM TIME CONSTANT

One of the advantages of the condenser, cited above, is the saving of time in shifting from lead to lead. If the time constant is long, this advantage disappears, since it may require the lapse of a considerable period of time for the string to reach its normal position after a shift of leads. The time required is proportional to the time constant and to the difference in the constant voltage (skin current) between the two leads. Too long a time constant, therefore, entails a loss of the advantages of the condenser.

It is desirable to arrive at a minimum time constant which will not cause distortion of clinical significance. With the help of the

Fig. 6.—An extreme case in which there is measurable distortion even for a time constant of 2 seconds: *A*, no condenser; *B*, $\tau = 3$ sec.; *C*, $\tau = 2$ sec.; *D*, $\tau = 1$ sec.; *E*, $\tau = 0.5$; *F*, $\tau = 0.1$ sec.

formula for determining the depression at the end of a wave, we may reason as follows. The most important clinical distortion is the depression of the RS-T segment. With an R-wave of 0.1 second or less in duration, and 20 mm. or less in height, a time constant of 2.0 seconds would introduce a depression of the RS-T segment of 0.5 mm. or less. Therefore, 2.0 seconds is perhaps the optimum value for the time constant.

Even with a 2.0 second time constant there may, in exceptional cases, still remain some distortion of possible clinical significance. Fig. 6 shows a series of electrocardiograms taken on an actual patient with and without condensers. Various time constants were used as indicated.

With a 2.0 second time constant there is an increase in the elevation of the T take-off by 0.6 mm., which may still be significant. Hence in such an exceptional case (high and wide wave) an even longer time constant is necessary for distortionless recording, or the calcu-

lated value for the overshooting should be deducted from the observed deviation to arrive at the real value.

USE OF THE CONDENSER WITH STRING GALVANOMETER

In case ease of shifting leads is of importance, the condenser in the string galvanometer must be connected at a point in the circuit beyond the lead changing switch. The string protecting switch (short-circuiting type) should be connected so that it will not short circuit the condenser through the string. With these connections properly made, switching from lead to lead involves only three motions. First, the string protection is put on; second, the lead is changed; and third, the string protection is removed. With a skin voltage difference between two leads of 15 millivolts and with 500 mf. (3.5 second time constant) the string protection must be left on for six seconds in order that the string may be practically at the center of the field when the protection is removed. For other conditions the time may easily be computed, as it is proportional to the time constant and the difference in skin voltage.

Paper condensers of large capacity are expensive, heavy, and bulky. It is possible to use electrolytic condensers which reduce the expense, the size and weight considerably. They must be connected in such a way that the normal polarizing voltages found in such condensers may be neutralized. This can be done by connecting them in a bridge arrangement. By this means a satisfactory condenser of 500 mf. may be constructed which will weigh about 5 pounds and occupy a space of only $8'' \times 7'' \times 6''$.

When using the condenser, it is desirable to use short-circuiting string protection such as is used in most of the more recent string electrocardiographs.

The most important uses for the condenser are as follows:

1. For taking one lead over a long period of time without watching the string. Adventitious movements will not throw the string off the field. The tracing will go along evenly, it will look better, and will be easier to read.

2. For use when only an untrained assistant is available. A trained person can set up the machine and an untrained individual may then operate it.

3. For taking tracings of the three leads where rapid shifting from lead to lead is necessary, and time relationships rather than the fine details of the form of the electrocardiogram are being studied. In this case a condenser of relatively low capacity should be used. Such records may be corrected by the use of the formulas given above.

SUMMARY

1. Condensers placed in the string galvanometer or amplifier type of electrocardiograph make compensation for "skin current" auto-

matic. String galvanometers are not ordinarily equipped with condensers; whereas most amplifier electrocardiographs are so equipped.

2. The presence of condensers introduces distortion.

3. The chief distortions that may be introduced by condensers in the electrocardiograph in clinical practice are RS-T deviation and diminution in the height of the R-wave. Since attention is paid to the RS-T segment in the diagnosis of coronary artery disease, rheumatic fever, etc., its deviation is significant. The time relationships are unaltered.

4. The magnitude of the distortion is proportional to the duration and amplitude of the wave being recorded and is also, in a simple circuit (string galvanometer), inversely proportional to the product of the resistance and capacity.

5. This product is known as the time constant. An amplifier circuit (which is a series of simple circuits) has an equivalent time constant to which the distortion is likewise inversely proportional. A simple method is given for determining this constant.

6. Formulas are given for determining the magnitude of the distortion.

7. If the time constant of the circuit is 2.0 seconds or more, the distortion is not usually significant in clinical practice.

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A SELF-RETAINING SKIN CONTACT ELECTRODE FOR CHEST LEADS IN ELECTROCARDIOGRAPHY*

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SINCE the introduction of the electrocardiographic Lead IV by Wolferth and Wood in January, 1932, the study of chest leads has taken on considerable impetus. Many workers are now investigating the subject with the hope of finding some lead or leads that will disclose evidences of myocardial damage not revealed by the standard three leads originally adopted by Einthoven for clinical electrocardiography. In

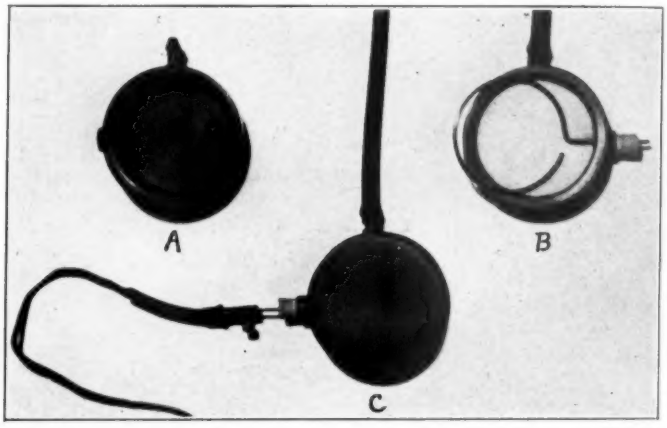

Fig. 1.—*A*, hard rubber cup (described in text). *B*. Electrode partly assembled; bottom of cup contains moist wool pad and copper loop is partly in place. *C*, Completely assembled electrode.

the successful pursuit of the study of chest leads, one requires a suitable electrode which will satisfy the following requirements:

1. That the electrode cover a *small surface*, to enable the investigator to "tap" the "potential" over selected small areas. This is essential because the potentials over the chest wall vary appreciably from point to point, even when these are one or two inches apart.

2. That the electrode be *completely insulated*. This is to prevent contact with adjacent areas of skin or other sources of extraneous potentials.

3. That the electrode *retain its position* absolutely. A sliding electrode may produce artifacts.

4. That the electrode offer a *low resistance* to the circuit. Overshooting of the galvanometer string is to be avoided if we are to evaluate

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tracings of chest leads, particularly during this initial stage of our investigation of chest leads.

With these requirements in mind I have constructed an electrode, illustrated in Fig. 1. It consists of a hard rubber cup, about a half inch deep and about one and three-quarter inches in diameter.* Within the cup there is a copper loop between two pads of wool. The free end of the copper loop protrudes through an opening in the side of the cup. A small perforated rubber stopper slides over the end of the wire. This stopper fits the opening in the side of the cup and serves to seal the exit of the wire. Into another opening in the side of the cup there is fitted a small nozzle to which a rubber tube is attached for the purpose of producing a partial vacuum within the cup, when in use. An elastic band is stretched over the free margin of the cup with sufficient overlapping to keep the contents in place.

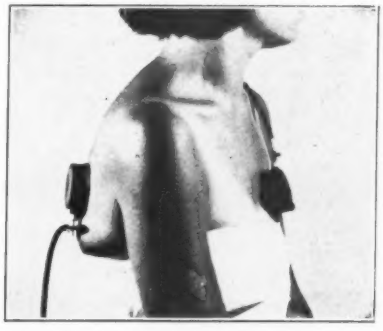

Fig. 2.—Electrodes in situ, retaining their position on chest wall.

METHOD OF ASSEMBLING ELECTRODE AND APPLYING IT TO THE CHEST WALL

1. Place one *moist* wool pad into cup.

2. Introduce copper loop, with free end protruding through opening in the side of the cup.

3. Holding loop in place with thumb, slip perforated rubber stopper over free end of wire, and by gentle rotation, force stopper into opening of cup and press it firmly into place. To test whether stopper has sealed opening, invert cup over palm of hand, press firmly and make slight suction on nozzle. If stopper is firmly in place, such suction must produce a partial vacuum sufficient to hold cup against palm.

4. Place a second *moist* wool pad into cup.

5. Stretch elastic band over free margin of cup with sufficient overlapping to hold contents in place (elastic band should overlap about one-eighth inch).

*The set consists of three electrodes. Two of these have dimensions as specified above. The third is smaller—surface diameter only one and one-quarter inches. This is useful in case one wishes a more accurate localization in the region of the apex impulse of the heart.

With proper preparation of skin, these smaller electrodes may be used exclusively.

6. Put assembled electrode into warm (not hot) salt solution, from three to five minutes.

7. Select area on chest wall where electrodes are to be applied.

8. Cleanse area with water and alcohol and rub vigorously with moist coarse cloth until skin is flushed (if skin is too thick and cannot produce flush, one may make a small superficial scratch with a dull, sterile needle point).

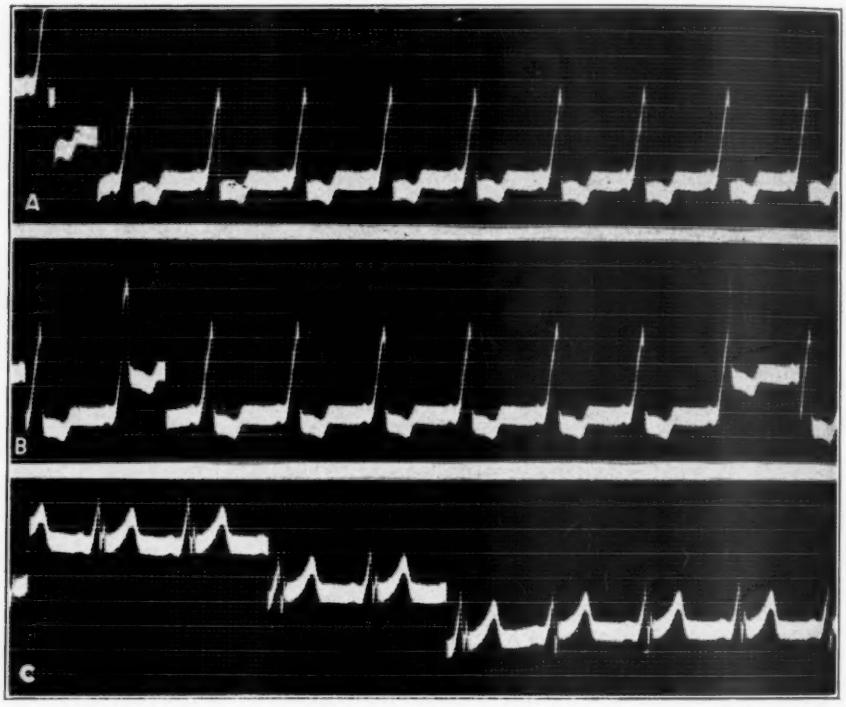

Fig. 3.—*A*, Conventional Lead I taken in usual manner, large surface contact, salt water bandages containing a large German silver plate. *B*, Conventional Lead I taken with electrodes here described, held in place over the anterior surfaces of right and left forearms. *C*, Chest lead taken with self-retaining electrodes of one and three-quarter inches surface area. The right electrode was applied one inch above and mesad to angle of right scapula. The left electrode was applied three inches lateral to left sternal margin in fourth interspace.

9. Remove electrodes from salt solution; express excessive water; wipe cup dry, especially protruding wire; make contact between end of copper wire and "lead" cable; attach soft rubber tube to nozzle.

10. Place cup over selected area; press firmly against chest wall. While pressing, produce partial vacuum through rubber tube (use medium-sized syringe and produce vacuum sufficient to collapse rubber tube). Clamp tube. Proceed to take the electrocardiogram (see Fig. 2).

CAUTIONS TO BE OBSERVED

1. Do not permit cable to drag on the electrodes.

2. Patient should be relaxed and cautioned not to move about, lest he stretch his skin and dislodge electrodes.

3. In case of male patients, the area selected may have to be shaved.

4. Copper loops must be clean. Scrape before using, or replace by new one frequently.

5. After electrocardiogram has been recorded, electrodes should be taken apart, being careful not to bend copper loop when removing rubber stopper. Parts should be washed and dried so as not to permit the accumulation of salt crystals.

6. *Never boil* hard rubber cup. Hot water will distort it.

The instrument is essentially a vacuum cup containing the electrode. As such, after it has been applied for some time it may leave a hyperemic zone which, for cosmetic reasons, may be undesirable on the part of some patients. In such a case the electrode may be used without suction. It can be applied to the chest wall in the same manner as one would apply a stethoscope bell. If the skin is prepared, satisfactory tracings can be taken in this way. An assistant or the patient himself may hold the electrodes in place.

The resistance with these electrodes may safely range from 1 to 4000 ohms without overshooting of the galvanometer string. Higher resistances have been found satisfactory, but as a general rule they should be avoided.

Tracings taken with these electrodes are shown in Fig. 3. Fig. 3*A* shows tracings taken in the usual manner—large plates and salt water bandages. Resistance, 1500 ohms. Fig. 3*B* shows tracing taken from extremities with self-retaining small electrodes. Resistance, 2500 ohms. Fig. 3*C* shows chest lead from same patient. Resistance, 750 ohms.

SUMMARY

A new skin contact electrode for electrocardiographic work is presented. This electrode is of small surface, completely insulated, of low resistance and is self-retaining. It is hoped that it will facilitate in particular the study of chest leads in electrocardiography.

AN EFFICIENT APPARATUS FOR SIMULTANEOUS ELECTROCARDIOGRAPHIC AND ARTERIAL PULSE RECORDS*

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University, Va.

ARTERIAL pulse curves are not infrequently of value, especially in medical teaching. Combined electrocardiographic and arterial pulse records often serve to elucidate the various cardiac arrhythmias. Difficulties attendant upon the proper recording of simultaneous arterial and electrocardiographic curves are based partly upon inefficiency of

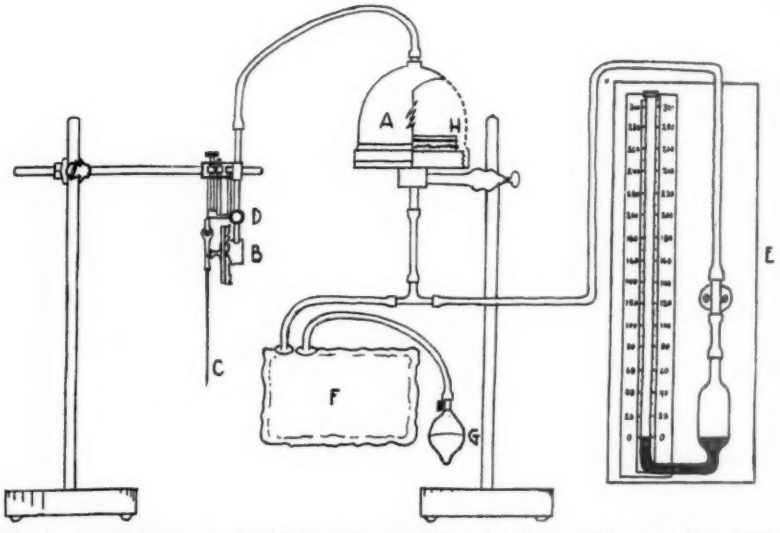

Fig. 1.—A, Erlanger metal bell. B. recording tambour with recording lever C and escape valve D. E, mercury manometer. F, clinical blood pressure cuff with usual bulb and valve G.

the average receiving tambour or glycerin pellote and occasionally upon the observer's lack of familiarity with their use. The apparatus described below obviates both of these difficulties as it requires no particular adjustment and invariably permits a good excursion of the arterial recording lever. Application of a clinical blood pressure cuff is the only adjustment necessary for reception of the arterial impulse when used with an Erlanger bell, and a recording tambour. The cuff may be pumped up and left in place so that one person may operate both galvanometer and arterial lever and easily obtain a double record (Fig. 2*a*). While a combination of the Erlanger capsule with arterial pulse levers has been previously suggested,[1] it is thought that the particular arrangement indicated below will be useful and therefore worthy of description.

*From the Department of Internal Medicine, School of Medicine, University of Virginia, University, Va.

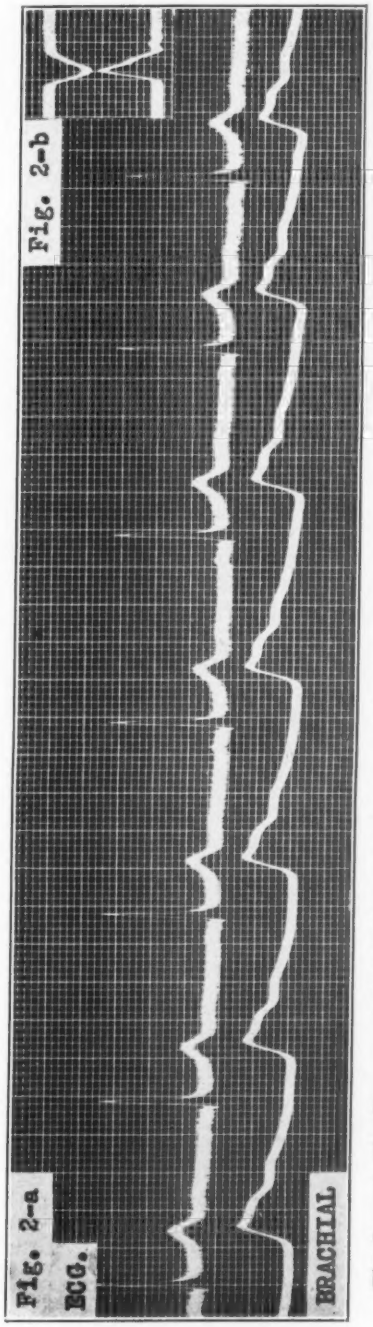

Fig. 2.—(a) Simultaneous electrocardiogram, Lead II, and brachial pulse curve from right arm. The arterial curve is displaced to the right by approximately 0.026 second. (b) Record of delay from cuff F to recording lever C. For method of calculation see text.

APPARATUS AND METHOD

The accompanying diagram (Fig. 1) is practically self-explanatory. An Erlanger metal bell (A), the base (H) of which has been covered

with three layers of rubber dam, is placed between an ordinary clinical blood pressure cuff (F) and simple recording tambour (B). Clinical mercury manometer (E) is attached on the cuff side of the system by a T-tube. Light broom straw recording lever (C) is placed vertically in front of the camera aperture of the electrocardiograph. Electrodes are attached as usual, the blood pressure cuff is applied to the arm, pumped to the approximate diastolic pressure of the patient, and the tracing taken. The resulting curves are smoother and of a more usual contour if a slight air escape is allowed in the recording tambour at valve (D).

The best excursions of the arterial recording tambour have been obtained when three layers of rubber dam (weight, approximately 1.1 oz. per sq. ft.) have been used at H. A single layer of much lighter rubber membrane should be used on tambour (B).

ERROR AND CORRECTION

Delay in the air system between cuff (F) and recording lever (C) has been calculated by a simple and direct method. Cuff (F) is rolled up tightly, a light broom straw placed between its folds with four or five cm. of broom straw projecting beyond the edge of the cuff. The rolled cuff is then placed in a claw clamp and adjusted so that the shadow of the projecting broom straw will fall on the camera aperture parallel to recording lever (C). If the cuff is then pumped up to 80 mm. Hg and compressed sharply with thumb and forefinger, there is an immediate movement of the straw held tightly in its partially distended folds and a corresponding response of lever (C). Movement of the broom straw in cuff and the resultant movement of lever (C) may be photographed with the electrocardiographic camera, and the delay from cuff (F) to lever (C) indicated. For example, from the beginning of the upper curve of Fig. 2*b* to the beginning of the lower curve there is a delay of approximately 0.026 sec., as measured with a Cambridge Record Measurer. The brachial curve shown in Fig. 2*a* is therefore displaced to the right by this interval. Thus the apparatus does not exceed in error instruments previously used; Lewis[2] has stated the delay in transmission through the air of the rubber tubing to be approximately 0.03 sec. in the radial and brachial curves shown in his book. Ordinarily the patient may be placed close to the galvanometer so that the distance from the cuff to recording tambour is not more than two or three feet. However, satisfactory tracings may be obtained with the patient as far away as nine or ten feet from the instrument, with a slight additional delay in the arterial record.

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Department of Clinical Reports

COARCTATION OF THE AORTA*

Report of a Case in Which Sudden Death Was Due to Rupture of the Aorta

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THE embryology, pathological anatomy, clinical features, and pathological physiology of coarctation of the aorta as well as the roentgenographic findings in cases have been reported on in detail, not only in Abbott's classical contribution to this subject, but also in the papers of King,[12] Woltman and Shelden,[18] Rösler,[15] Blackford,[1] Railsback and Dock,[14] Thomson and Lamb,[16] Fray,[8] Ernstene and Robins,[5] Blumgart, Lawrence and Ernstene,[2] Lemon,[13] East,[3] Hampson,[10] Ulrich,[7] Evans,[6] and Eppinger and Midelfart.[4] The object of the present communication is to report a case in which death was due to rupture of the aorta following a dissecting aneurysm. In addition some studies of the arteries above and below the point of coarctation were made to determine the effect of the wide variation in pressure upon these vessels.

J. W., a white male, aged twenty-six years, an Italian laborer, was admitted to Jefferson Hospital in a state of shock. He had always been healthy and recalled no illnesses, aside from slight colds. The family history contained nothing of note. On November 14, 1930, the patient went to work feeling quite well. While carrying a heavy timber he was seized with pain in the "pit of the stomach." This was so severe that he was compelled to drop his burden. He nevertheless continued to work for several hours, although still experiencing severe pain in the upper abdomen. He remained in bed for two days, following which the pain gradually subsided. On November 17 he returned to work, feeling better, although his discomfort had not entirely disappeared. Upon lifting a heavy block of wood he was again seized with a pain which was so much more severe and agonizing than that previously experienced that he collapsed. He was brought to the hospital in a state of shock but was able to answer questions.

The pain was localized in the lower left chest and upper abdomen and was aggravated by deep inspiration. Examination revealed a well-developed adult male with shallow respirations. There were visible pulsations of the vessels of the neck. The chest appeared distended over the lower left anterior portion. The heart was slightly enlarged in the transverse diameter; the sounds were of good quality, and a systolic murmur was audible at the apex. The pulse was regular, the rate ranging from 90 to 112. The blood pressure in the right arm ranged from 126/60 to

*From the Laboratories of Pathology of the Jefferson Medical College and Hospital and the Philadelphia General Hospital aided by the Martin Research Fund.

136/60. The blood pressure of the legs was not recorded. A slight bulge was observed in the upper left quadrant of the abdomen, and the rectus muscle in this region was extremely tender and rigid. No masses were palpable.

The day following admission he appeared fairly comfortable under morphine. His temperature, which was normal on admission, rapidly rose to 102°. His pulse ranged from 90 to 112 and respirations from 20 to 24 per minute. Blood count and blood chemistry were normal. The urine showed a trace of albumin and hyaline casts. Blood Wassermann reaction was negative, and the icterus index was 9.2. The patient was in the hospital but two days, and his condition was so grave that complete studies were not made. Death occurred suddenly at 1 A.M. on November 19. The diagnostic impression was that of an acute cardiac or intraabdominal calamity, the exact nature of which was not determined.

Post-mortem Examination.—The chief findings of interest were confined to the heart, aorta and its branches. The pericardial sac contained 700 c.c. of partially

Fig. 1.—Heart showing upper portion of ventricular septum (left) with aorta attached; (1) subaortic stenosis; (2) irregularly widened aortic cusp; (3) aortic tear just above cusps; (4) dissection aneurysm; (5) point of coarctation.

clotted blood. The heart was definitely enlarged, its weight being 870 gm. Both ventricles were dilated and hypertrophied, this being more marked in the left ventricle. The musculature, however, appeared normal in color and consistency. The left ventricular wall at its midportion measured 25 mm., the right 8 mm., the mitral valve measured 8 cm., pulmonic 7.5 cm., the tricuspid 12 cm. and the aortic 8.1 cm. The cusps of the aortic valve varied somewhat in width; the right anterior measured 3.1 cm. and the left 2.6 cm.; the posterior 2.4 cm. at the free margin. A moderate subaortic stenosis was present. The ascending aorta was dilated and tended to form a distinct aneurysmal sac. The aorta 3 cm. from its origin measured 8.4 cm.; 6 cm. from its origin 7.5 cm. Immediately above the right anterior leaflet was a complete semicircular tear in the aorta measuring 2.5 cm. in its longest diameter (Fig. 1). A fresh thrombus protruded through the point of rupture and extended into the pericardial sac. Beginning at the origin of the aorta was a dissecting aneurysm which extended upward between the media and adventitia

of the ascending and transverse portion and separated the corresponding coats of its main branches. Twelve cm. from the origin of the aorta and immediately below the insertion of the ductus arteriosus was an almost complete obliteration of its lumen. The marked stenosis was the result of narrowing at that point and in addition of the interposition of a smooth fibrous diaphragm which was concave toward the heart and convex toward the thoracic aorta, ending in a small papilla which admitted only the passage of a bristle. The openings of the innominate, left common carotid and left subclavian arteries were considerably dilated and the vessels thickened and tortuous. The internal mammary and the other arteries arising from the subclavian trunk, particularly on the right, were also dilated, thickened and tortuous. The lumen of the aorta was small and its wall much thinner below the point of coarctation. The openings of the first aortic intercostals were small, but those of the second, third, fourth, fifth, sixth and the bronchial, together with the other branches of the abdominal aorta, were markedly dilated. There was no evidence of atherosclerosis or syphilis.

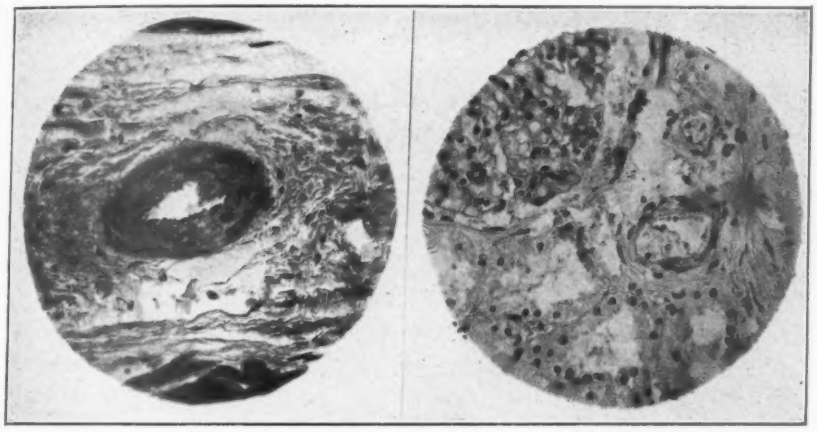

Fig. 2. Fig. 3.

Fig. 2.—Small arteriole in myocardium. Note relation between thickness of vessel wall and diameter of lumen. Compare with Fig. 3.

Fig. 3.—Two small arterial branches in the kidney. Note relation between thickness of vessel wall and diameter of lumen. Compare with Fig. 2.

Microscopic Examination.—Thin pieces of the various tissues were fixed in 10 per cent formalin and Zenker's fluid. They were cut and stained with hematoxylin and eosin, Mallory's and van Gieson's connective tissue stains, Verhoeff's stain for elastic tissue and phosphotungstic acid stain for fibroglia. The heart muscle showed evidence of hypertrophy of its fibers and slight granular degeneration. The chief finding of interest was the marked thickening of the walls of the smaller sized arteries. (Fig. 2.) This hypertrophy involved musculature as well as internal elastic lamina. The larger branches of the pulmonary artery were unchanged. The smaller ones showed hyperplasia, reduplication and fraying of the internal elastic lamina. The branches of the bronchial arteries were unchanged. The smaller arteries and arterioles in the organs supplied by the aorta below the point of coarctation were normal (Fig. 3).

Sections of the aorta just above the cusps and proximal to the tear showed marked thickening of the vasa vasorum. Red cells, many large polyblasts and a few fibroblasts were seen lying between the layers of the media and adventitia and between the frayed muscle fibers of the media which contained quite a considerable

amount of basophilic ground substance in which the collagenous fibers were embedded and which was areolar in arrangement. The elastica of the inner portion of the media was fairly well intact, although that in the outer portion of the media was considerably frayed and broken up. Sections from the torn flap of the aorta showed in addition to the changes just described an enormous amount of fluid and blood especially in the media and also between the intima and the media, necrosis of the media, extensive interruption of all the elastic tissue and an increase in collagen in the inner fifth of the media. Sections from the descending thoracic aorta below the point of coaretation showed that part of the vessel to be thin due to medial hypoplasia; the inner portion of the intima had a vacuolated appearance and showed considerable metachromatic connective tissue which stained red with van Gieson's stain.

The pathological diagnosis was coaretation of the aorta of the adult type; cardiac enlargement due chiefly to hypertrophy; subaortic stenosis; unequal width of aortic cusps; aneurysmal dilatation of ascending aorta; dissecting aneurysm with rupture; hemopericardium; hypoplasia of the aorta distal to point of coarctation; passive congestion of the liver, spleen and kidneys; hypertrophy of the media and of the internal elastic lamina of the branches of the coronary arteries and arterioles; hyperplastic sclerosis of the small branches of the pulmonary artery.

COMMENT

The presence of the thickened arterioles observed in the heart is worthy of discussion. Although the systolic blood pressure reported in this case was 136 mm., this was obtained while the patient was in a state of shock; and from our knowledge of these cases, together with the cardiac enlargement observed, it seems reasonable to suppose that his blood pressure before the accident was considerably higher. Hypertension above the point of coaretation had probably been present for many years. In long standing, essential hypertension the associated sclerotic lesions of the smaller branches of the renal arteries and of similar vessels elsewhere, is believed by many to be the result of hypertension, although this point has not definitely been settled. In the case of coaretation, it is interesting to study this point because the patients have a high blood pressure proximal to the coaretation and a low blood pressure distally. It is interesting to observe the effect of hypertension in one part of the body and a normal or lower tension in the remaining portion in the same individual. Hypertrophy of the media and internal elastica in the smaller arteries is considered to be a stage of arteriosclerosis (Fishberg;[7] Kernohan, Anderson and Keith[11]). This finding in a person of twenty-five years with normal caliber of arterioles in the organ distal to the coaretation, in the absence of other obvious etiology, would suggest that the hypertension was possibly a factor in its production. The thickening of the coronary arteries and arterioles may possibly be the result of the high blood pressure existing above the point of coaretation, although the evidence presented is admittedly too inconclusive to justify a definite causal relationship. Unfortunately the arterioles of other tissues above the site of coaretation were not studied from this standpoint. If this

hypertension was productive of these arterial changes, it is conceivable that its longer duration would result in more definite sclerotic lesions. In spite of the high systolic pressure above the point of coarctation and a lower pressure below, there is no conclusive evidence that sclerotic changes in the vessels are more marked above the point of constriction. Occasionally the vessels below the point of coarctation have shown more sclerosis than those above.[16]

In Hamilton and Abbott's[9] latest series of 200 cases of coarctation there were but 33 in which rupture of the aorta occurred proximal to the point of coarctation. In two cases, rupture of the heart itself occurred, and in five rupture of the aorta was below the point of coarctation. In the great majority of their series, this tear, as in our case, led to a dissecting aneurysm which extended from between the layers of the media or the media and adventitia, and ruptured secondarily hours or days after the primary intimal tear. There were apparently but few cases where the tear occurred through all the coats of the vessel with death following immediately.

A dilatation of the ascending aorta, as was present in our case, was observed in 101 out of the 200 cases of their series; in 71 this point was not mentioned. Cardiac hypertrophy, especially of the left ventricle, is extremely common and was noted in 150 of their cases. However, cardiac hypertrophy was not necessarily present and was absent in some of the older patients. In 108 of their series the stenosis resembled or approached that observed in our case; i.e., the opening was reduced to a very small lumen ranging in diameter from 6 mm. to one so minute as to allow the passage of a hair or bristle. In 47 of the 200 cases the stenosis was complete. It is interesting to note the causes of death in coarctation. Spontaneous rupture of the aorta or heart occurred in 40 cases; 24 patients died from a cerebral lesion, usually hemorrhage; 60 from cardiac decompensation and 17 without apparent cause.

SUMMARY

A case of coarctation occurring in an apparently healthy young adult is reported in which death was due to rupture of the aorta.

The possible relation of hypertension to arteriosclerosis is discussed.

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SCLEROSIS OF THE CORONARY ARTERIES WITH MYOCARDIAL INFARCTION IN A YOUNG WOMAN

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WAVERLY, IOWA

ARTERIOSCLEROTIC heart disease in men under forty years of age has been mentioned in the literature on numerous occasions, but the condition is apparently rarely encountered in women of this age period. Levine[1] in his monograph reported three young adults, one of whom was a woman thirty-nine years old. Willius and Brown[2] describe the case of a woman thirty-five years of age with angina pectoris and myocardial failure, who died suddenly. Although a necropsy was not performed, the clinical manifestations justified the diagnosis of coronary artery disease. Wolff and White[3] cite a case from the literature of a young woman twenty-one years of age in whom a diagnosis of coronary artery disease was confirmed by necropsy.

The following case report concerns a woman who at the onset of her symptoms was thirty-two years old. When she was first seen, it was felt that a sclerosis of the coronary vessels was probably responsible for her cardiac disability. The age of the individual, the presence of a nodular goiter and the subsequent course suggesting infection, however, made this diagnosis uncertain.

CASE REPORT

Mrs. J. R. M., white, aged thirty-three years, was admitted to the hospital for examination October 27, 1932.

History.—She complained of nervousness, weakness, shortness of breath on exertion, attacks of choking sensation during the night, and cough.

The onset of the symptoms dated back to about two months prior to the birth of her last child in April, 1932. At this time she noted that she became unusually short of breath on exertion. The labor was normal, and following this there were no particular complaints until July of the same year. She began to experience shortness of breath on exertion, became fatigued easily, and in a short time became very nervous. These symptoms gradually progressed, and in September nocturnal dyspnea appeared. The latter was described as attacks of choking sensation which would awaken her from sleep and compel her to sit up in bed to get her breath. When first seen about one month later she complained chiefly of the dyspnea and a nonproductive cough. The nocturnal attacks gradually increased in frequency and in severity. There was no history of pain suggestive of the anginal type. She stated she had lost about 30 pounds in weight during the past four months, the present weight being 176 pounds.

She apparently had not been strong as a child, but according to her history had had no significant illness aside from a severe attack of scarlet fever at twenty-two years of age. She was not aware of any cardiac involvement from the scarlet fever. A careful inquiry was made concerning rheumatic infection, and with the possible

exception of growing pains at the age of twelve years, the history from this standpoint was negative. She was married at twenty-three years and weighed 125 pounds. Six months after the birth of her first child her weight had increased to 170 pounds. She had two children who were living and well and had had no miscarriages. Both pregnancies were carefully followed, and at no time was there any elevation of the blood pressure.

The father and mother, two brothers and two sisters were alive and well. On the paternal side there was a history of several cousins having died from heart disease, but the basis of the cardiac disability was not known.

Findings.—The patient was moderately obese and well developed. Pupils reacted promptly to light and accommodation. There was a moderate sclerosis of the retinal vessels. The teeth appeared to be in good condition and except for an enlargement of the right tonsil nothing of particular importance was noted in the examination of the nose and throat. There was a moderate nodular enlargement of the thyroid gland. The lungs were apparently clear. In the examination of the heart the muffled cardiac tones and the gallop rhythm were the most conspicuous features. The left border of the heart was just outside the midclavicular line and there were no definite murmurs. The systolic blood pressure was 119 mm. and the diastolic 92 mm. The pulse was of the low tension type, and there were no significant alterations in the walls of the peripheral vessels. The liver was enlarged, extending a hand'sbreadth below the costal margin and was moderately tender. There was no peripheral edema. The blood picture was that of a mild secondary anemia and the urine was negative. In the teleroentgenogram the transverse diameter of the heart was 16.5 cm. and the transverse thoracic diameter was 28 cm. The blood Wassermann was negative. The basal metabolic rate was minus 10 per cent.

Clinical Course.—In spite of periods of absolute bed rest, promotion of relaxation and sleep and various additional therapeutic measures, the clinical course was progressively downward. The dyspnea became a very prominent feature with distressing periods of orthopnea, and in time anasarca developed. There was no particular alteration in the blood pressure, and the cardiac rhythm was regular except for an occasional auricular and ventricular premature contraction. The heart sounds gradually became distant and the gallop rhythm more conspicuous. The electrocardiogram taken at the time of the first examination presented a left axis deviation with a slight slurring and some increase in the duration of the QRS complex. Later there was a gradual reduction in the amplitude of the chief ventricular deflection. The patient died March 3, 1933.

Pathological Report.—(The autopsy was limited to the examination of the heart.) The heart weighed 400 gm. There was a rather extensive dilatation of the left ventricle with a mural thrombus in the left ventricle and right auricle. The myocardium presented a moderate degree of fibrosis involving particularly the subendocardial layers of the left ventricle. The changes in the coronary arteries involved particularly the smaller branches as shown in the microscopic sections.

Histological examination: Sections were taken from the anterior wall of the left ventricle, apex of the left ventricle, the interventricular septum and the right auricle. In the section from the anterior wall of the left ventricle there was an absence of the cross striations of the subendocardial muscle cells, and these fibers were swollen and stained pale blue. One area of the endocardium showed an adherent and partially organized thrombus. Several small areas of infarction, acute, subacute and old were seen. Over the entire section the muscle fibers appeared somewhat atrophic and the vessels were thickened. Two of these vessels showed partially organized thrombi. In the section taken from the apex of the left ventricle the mural thrombus was considerably thicker than that presented in the above section. The cardiac musculature likewise showed varying degrees of degen-

eration. In the section from the interventricular septum there was a rather extensive degeneration of the muscle cells with young fibrous tissue proliferation. The section from the right auricle was composed largely of organized thrombus. The auricular muscle stained poorly and showed some vacuolization.

COMMENT

The above case report is that of a young woman in whom the clinical diagnosis of probable coronary artery disease was verified by necropsy. The histological examination showed extensive degenerative changes in the myocardium, secondary to sclerosis and occlusion of certain of the smaller coronary vessels.

While sclerosis of the coronary arteries producing cardiac disability is rare in women of this age, the possibility must be borne in mind, particularly in the absence of other etiological factors. In this patient the presence of a nodular goiter directed attention to the possibility of a thyrotoxicosis, but at no time were there any apparent clinical manifestations of this condition.

Note.—I wish to acknowledge my indebtedness to Dr. J. W. Kernohan of the Department of Pathology, Mayo Clinic, for the pathological report.

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Correspondence

A Plea for Uniformity in the Biological Standardization of Commercial Preparations of Digitalis

To the Editor of the American Heart Journal:

The chemistry of the digitalis glucosides is, as yet, but imperfectly understood. Chemical assay is therefore not feasible, and it is necessary to resort to the technic of biological standardization. Most of the digitalis products now marketed in America are so standardized.

The present situation with respect to the biological assay of digitalis is unsatisfactory both to practitioners of medicine and to the manufacturing drug firms. The various factors which lead to confusion are as follows:

1. The one-hour frog method is official in the Pharmacopeia of the United States.

2. Other methods of assay have been devised, and one or another of these is employed for the standardization of commercial products, e.g., the cat method of Hatcher and Brody, the guinea-pig method of Vanderkleed, and the Magnus modification of the Hatcher-Brody technic. The establishment of an international unit has also been attempted, and at least one firm markets a preparation said to be assayed in terms of this unit.

3. There is abundant evidence which indicates that the cat method of Hatcher and Brody yields uniform and reliable results, and that the relative potencies of different preparations, as determined by this method, apply to human dosage. When a specimen is found to be twice as active as another by this method, it is also twice as active in man.

4. No standard of potency has been established for preparations that are assayed by the cat method. Thus, 1 c.c. of a given tincture may contain the equivalent of ½ cat unit; 1 c.c. of another tincture may contain 2 cat units. Tablets, pills and capsules vary in like fashion.

When the physician prescribes digitalis, he is entitled to receive a dependable and uniform product. The drug manufacturer requires, and is anxious for, guidance and support from the medical profession. He is confronted on the one hand by the U. S. Pharmacopeia, which sets its stamp of approval upon the frog unit; and on the other hand, by a majority of competent cardiologists and pharmacologists, who favor the use of the cat unit.

The Heart Committee of the New York Tuberculosis and Health Association has, for a number of years, distributed to its constituent cardiac

clinics tablets of digitalis leaf standardized by the cat method of Hatcher and Brody. The tablets have been made up to the strength of one cat unit, one-half cat unit, and two cat units. The experience with this preparation has been entirely satisfactory.

On the basis of the facts cited, the following recommendations are made by the Heart Committee of the New York Tuberculosis and Health Association:

1. For the present, and until further knowledge may necessitate a change in point of view, digitalis preparations should be standardized by the cat method of Hatcher and Brody. For convenience the exact procedure now followed in Dr. Hatcher's laboratory is appended.

2. In marketing commercial products, liquid preparations of digitalis should be put up so that 1 c.c. (15 minims) contains the equivalent of 1 cat unit.

3. In marketing tablets, pills or capsules of digitalis, each of these should contain the equivalent of 1 cat unit. Tablets, pills or capsules containing stated fractions or multiples of 1 cat unit may be dispensed, if desired.

It is hoped that the manufacturing drug firms will adopt these simple suggestions, for by so doing they will be rendering a real service to the members of the medical profession and their patients.

These recommendations have been approved by the Executive Committee of the American Heart Association.

APPENDIX

The cat method of Hatcher and Brody, as carried out in the Department of Pharmacology of the Cornell University Medical College, is as follows:

The digitalis leaf to be assayed is first made up into a tincture, in accordance with the directions given in the U. S. Pharmacopeia. The tincture is then diluted twenty times with physiological salt solution. The diluted tincture is injected slowly and continuously from a burette into the saphenous vein of the cat until death results from ventricular fibrillation. The rate of injection is such that the total dose is injected in about ninety minutes. The test may be made during light ether anesthesia; or only local anesthesia may be employed, 1 per cent novocaine being injected or 10 per cent phenol being rubbed into the skin for the exposure of the vein. Six cats are usually employed for one test. Pregnant, lactating or excessively fat animals are not used.

The cat unit potency of the preparation is the average of the results obtained with the group of animals and is expressed as the volume, in cubic centimeters, of undiluted tincture per kilogram of the animal required to cause death under the conditions described. The amount of leaf contained in this unit of tincture is readily calculated.

(Signed) Digitalis Committee.

Ernst P. Boas	Cary Eggleston	Harold E. B. Pardee
Alfred E. Cohn	Harry Gold	Homer F. Swift
Arthur C. de Graff	Bernard S. Oppenheimer	John Wyckoff

Robert L. Levy, Chairman.

Department of Reviews and Abstracts

Selected Abstracts

Clawson, B. J.: Relation of Allergy to General Resistance in Streptococcic Infection. J. Infect. Dis. **53**: 157, 1933.

A study of the relation of allergy to resistance was made in two series of animals. One group was rendered hypersensitive to streptococci, the other was made highly resistant to streptococci without the allergic state developing. The rate at which living streptococci were removed from the blood and liver following intravenous injections was compared in these two series and in normal animals. The height of the streptococcic agglutination titer was also compared in the three series of animals. It was found that organisms were not removed from the blood stream as rapidly in fifteen minutes in the allergic animals as in the normal animals. This suggested some harmful factor associated with the phenomenon of allergy. After two hours, however, a greater number of streptococci per gram of liver were killed in the allergic animals than in the normal animals. This difference was but a slight one. On the other hand, in the animals which were made resistant without allergy developing, organisms in the blood stream and in the liver were killed at a much greater rate than they were in either the normal or the allergic animals.

The findings in the experiments suggest that the allergic state is not necessary in the development of general protective resistance to streptococci. It even seems that allergy may be harmful from the standpoint of its effect on the phagocytic cells. It should not be said, probably, that allergy in general is a harmful concomitant phenomenon associated with resistance, for, from the standpoint of repair of tissues, allergy might be looked on as being useful, since the growth of connective tissue is stimulated. In the light of the foregoing experiments, it would seem that allergy bears no useful relation to general resistance in streptococcic infection, as indicated by phagocytosis, and that at times there may be a harmful relation.

Griffith, George C., Chamberlain, C. T., and Kitchell, J. R.: A Simplified Apparatus for Direct Venous Pressure Determination Modified From Moritz and V. Tabora. Am. J. M. Sc. **187**: 371, 1934.

A simple and inexpensive apparatus for venous pressure determination by the direct method of Moritz and v. Tabora is described together with the technic for its use. Attention is directed to the importance of estimating venous pressure in the diagnosis and treatment of cardiovascular disease.

Eyster, J. A. E., and Hicks, Earl V.: Effect of Respiration on Cardiac Output. Am. J. Physiol. **104**: 358, 1933.

In dogs under anesthesia in which stroke volume and minute cardiac output from the two ventricles is measured by a cardiometer during normal breathing, there occur during inspiration a diminished stroke volume and a slight fall of

right auricular pressure. The effective venous pressure is increased, since the fall in auricular pressure is not so great as the fall in intrathoracic pressure. The diminished total stroke volume may be explained by diminished left ventricular output due to retention of blood in the increased pulmonary bed.

In the greater reduction of intrathoracic pressure associated with the deep inspirations following vagus section, these effects are exaggerated, and in addition the diastolic volume is increased.

Under the conditions of these experiments, marked alterations of breathing have little effect on the average stroke volume or on minute volume when considered over a period of time. It is believed that the influence of the extent of breathing on venous return is not so great as is ordinarily stated.

Brams, W. A., Katz, L. H., and Kohn, L.: The Effect of Abdominal Distention and Release on the Blood Pressures in the Arteries and Veins. Am. J. Physiol. **104:** 120, 1933.

The effects of induction and release of abdominal distention on venous pressure, arterial pressure and cardiac stroke volume were studied in a series of 51 experiments.

The pressure in the inferior vena cava rose when the abdomen was distended while the pressure in the superior vena cava was slightly elevated or but little affected. Release of distention resulted in a prompt return of pressure in the inferior vena cava to normal. These results were approximately the same in experiments of short and long duration and in instances where distention was maintained for several days.

Arterial pressure fell in 27 of 48 experiments during distention of the abdomen and rose in 21 others. In 34 experiments a fall to a level below the normal occurred on abrupt release of abdominal distention. This was mirrored in the changes in stroke volume. The interplay of various factors responsible for these changes is discussed.

On release of distention of the abdomen a fall of arterial blood pressure was usually obtained. The fall in arterial pressure was 40 mm. of mercury in some instances and was sustained at that low level in a few.

The clinical importance of such a fall in arterial pressure on release of distention as a cause of syncope and death is discussed and adrenalin suggested as a rational form of treatment in the emergency.

Gregg, D. E., and Wiggers, C. J.: The Circulatory Effects of Acute Experimental Hypervolemia. Am. J. Physiol. **104:** 423, 1933.

The plasma and erythrocyte volumes of anesthetized dogs were increased experimentally by slow infusion of sedimented corpuscles during which pressure changes in the veins, ventricles and central arteries were followed, the latter two by use of optical manometers with a high figure of merit. In addition, alterations in urinary secretion, spleen volume, intrathoracic pressure, etc., were incidentally recorded.

The experiments demonstrated the following points: (1) While a considerable volume of blood can be accommodated by the dilatation of capillaries and venules in various blood reservoirs of the body, including the spleen, the maximum capacity available under normal conditions is not adequate to prevent an increased return to the heart during polycythemic hypervolemia. (2) The heart enclosed by its pericardium within the closed chest does not differ in its response from that of an exposed heart up to the limits imposed by very large increases in blood volumes. Evidence that the systolic discharge of the left ventricle increases is

given by the larger pulse pressure, the inordinate increase in the phases of isometric contraction and systolic ejection as well as by the contour changes exhibited by the pressure pulses. These are discussed. (3) Intraventricular pressure curves obtained from exposed hearts enclosed naturally within the pericardium indicate that initial tension increases considerably, thus supplying the force by which dilatation up to the capacity of the pericardial sac can be produced. The increased initial tension and length therefore represent the coefficients which determine the steeper gradient of the ventricular pressure pulses and the prolongation of systole. (4) During the early stages of hypervolemia, the increased systolic output is mainly responsible for the elevation of arterial pressure, for the gradients of the diastolic portion of the pressure curves do not change. This indicates that the increase in peripheral resistance occasioned by greater blood viscosity is nicely counterbalanced by dilatation of peripheral arterioles and widening of the capillary beds. These experiments supply no information as to whether this involves active changes in the caliber of peripheral vessels or is entirely passive. When the polycythemic hypervolemia becomes extreme, however, the effects of increased viscosity dominate and an increased peripheral resistance undoubtedly occurs. This is shown by the changing contour of the systolic portion of the pressure pulses and by a slower gradient of the diastolic decline as well.

Parkinson, John: The Radiology of Heart Disease. Brit. M. J. 2: 591, 1933.

In the modern diagnosis of cardiovascular disease, radiology takes an essential and important place comparable with that of electrocardiography. Radiology, when available, replaces percussion, for it is more accurate and informing and thus contributes to the progress of cardiology. Examination of a patient with doubtful or serious cardiac disease is incomplete unless it includes radiological examination. Diagnosis is confirmed and extended, and prognosis may be affected.

An anterior film alone is often inadequate. Radioscopy in the anterior and both oblique positions should be followed where necessary by teleradiograms in the anterior and left oblique, with or without the right oblique. Enlargement of the heart should not be diagnosed in the absence of an adequate cause and converging evidence unless radiological confirmation is obtained. Apparent enlargement is not infrequently due to scoliosis.

The difficulties surrounding the radiology of heart disease largely disappear if instead of looking for general enlargement, attention is centered upon the particular chambers or great vessels which may be modified in size, shape, or position.

Special care should be taken not to distress a patient by confronting him with x-ray findings as if they implied an additional diagnosis or a complication which magnified his disease.

Kerley, Peter: Radiology in Heart Disease. Brit. M. J. 2: 594, 1933.

This article describes briefly the technic of radiology of the heart and the findings in both normal hearts and those which are either small, enlarged, or which show changes in shape due to valve disease. The author also describes the findings in the lung due to hyperemia, edema and collapse, associated with heart disease.

Bramwell, Crighton: Radiological Diagnosis of Cardiac Enlargement. Brit. M. J. 2: 597, 1933.

The author believes that x-ray examination makes three important contributions to the diagnosis of pathological cardiac enlargement.

It can tell us all that we can learn from percussion and palpation regarding cardiac enlargement, and it can do so with a much higher degree of accuracy than either of these methods.

It can give us reliable information regarding slight changes in heart size and the slighter degrees of cardiac enlargement, even under the most unfavorable circumstances. Although slight cardiac enlargement by itself is not sufficient ground on which to base a diagnosis of heart disease, it may sway the balance when considered in conjunction with evidence from other sources.

X-ray examination can reveal changes in the shape of the heart outline. These changes tell us which chambers are enlarged and so indicate the probable cause of the enlargement. This is the most important contribution. The frontal silhouette alone gives us a far more accurate idea than does percussion of the shape of the heart, whereas examination in the two oblique positions yields additional information of which percussion can tell us little or nothing.

Rosenthal, Maurice: An Anatomic Mechanism in the Production of the Flint Murmur. Arch. Path. **16:** 862, 1933.

Two cases are presented in which a definite organic lesion not involving primarily the mitral valve seem to offer a definite and concrete explanation for the Flint murmur that was observed during the life of these two persons. Although the original and the previously given modified explanations of the mechanism of the Flint phenomenon are possible, they are not based on demonstrable pathological and anatomical changes; and this fact, associated with the vagueness of the clinical definition of the murmur, greatly weakens the value of this phenomenon for the clinician. If only one type of this murmur, therefore, can be established as caused by variation in anatomical structure, it would seem that it can be definitely removed from the group of poorly understood functional murmurs and included in that of the important organic murmurs of morphological significance. It is believed that one cause of the Flint murmur is a mechanical deformity or distortion of an otherwise essentially normal anterior flap of the mitral valve.

The deformity consists of a bulging of the anterior mitral leaflet with the formation of a culdesac on the auricular surface. This may be produced by vegetation on the posterior aortic cusp or by a calcified posterior cusp stiffened and fixed in its diastolic phase. Various aortic diseases may produce this deformity, such as bacterial infection, active or healed, arteriosclerosis and occasionally syphilis of the aorta, if it is complicated by secondary involvement and sclerosis of the aortic cusps.

Mackinnon, A. U.: The Rhythm of Paroxysmal Tachycardia. An Electrocardiographic Study. Quart. J. Med. **3:** 1, 1934.

The common type of paroxysmal ventricular tachycardia is markedly regular, and such irregularities as are present between consecutive beats are so slight as not to be appreciable by the human ear as departures from a regular rhythm.

Certain cases of auricular paroxysmal tachycardia may be clinically irregular. In the absence of the so-called Gallvardin's sign—the presence of a venous wave in the neck beating at a definitely slower rate than the ventricle—clinical irregularity in a typical paroxysmal tachycardia should not be held to indicate the presence of a ventricular origin until the electrocardiogram has proved the diagnosis beyond dispute.

As a general rule cases of auricular paroxysmal tachycardia have a greater degree of regularity than those tachycardias arising in the ventricle.

Irregularity in paroxysmal ventricular tachycardia may be due to: (1) con-

duction disturbances between focus and ventricle; (2) focal stimuli being too weak to excite the ventricle, or ventricular excitability so diminished that the ventricle does not respond to normal stimuli; (3) stimuli arising irregularly from a single focus; (4) stimuli arising irregularly from more than one focus in the ventricle.

Mohler, Henry K., and Crawford, Baxter L.: The Pathologic Changes in the Heart in Auricular Fibrillation. Am. J. M. Sc. **187**: 171, 1934.

The hearts of 15 fibrillators and 7 nonfibrillators having an etiology of rheumatic fever and mitral valve lesions were studied pathologically.

The hearts of 9 fibrillators with arteriosclerosis as the etiological factor were also studied. They had sclerotic changes in mitral valves in 7 with apparently normal valves in 2 cases.

There were no pathological changes common to all cases of auricular fibrillation found in this series of hearts. Nothing in this investigation indicates that the type of pathological lesion found at autopsy can of itself be responsible for the onset and continuation of auricular fibrillation. Etiological factors apparently determine the type of pathological changes to be found in the heart to a greater extent than does the presence or absence of fibrillation.

King, John T.: Bundle Branch Block. Am. J. M. Sc. **187**: 149, 1934.

An analysis of 155 instances of bundle-branch block in 150 patients is reported. In 17 cases in which autopsies were obtained a close correlation between clinical and pathological diagnoses was found. No attempt was made to determine the exact site of the lesion.

Most instances of bundle-branch block occur in association with degenerative heart disease; though a smaller number are found with about equal frequency in syphilitic or rheumatic infections of the heart. The proportion of cases is somewhat higher in general in rheumatic subjects than in syphilitic. Laborers are more prone to develop bundle-branch block than are professional men or housewives, while business men are neither predisposed nor immune. The condition is more common among men than among women.

In order of incidence, the important pathological disorders of cardiac mechanism may be listed as follows: auricular fibrillation, bundle-branch block, auriculoventricular heart-block, auricular flutter. First degree heart-block and complete A-V dissociation are found commonly associated with bundle-branch block. Bundle-branch block should be considered one of the rather common as well as important clinical entities. Various auscultatory phenomena encountered in bundle-branch block are recorded in diagrammatic form. It is emphasized that such signs are of less aid in establishing a diagnosis based on physical signs than are the surface movements of the cardiac apex.

The prognosis is very grave regardless of the etiology, though it appears best in those cases of rheumatic etiology. The occurrence of bundle-branch block seems to add nothing to the gravity of the prognosis of syphilitic heart disease. Since some individuals live for a considerable period with bundle-branch block, perhaps its presence should be looked upon as an omen of very grave import rather than as a necessarily fatal handicap.

Maher, C. C., Sullivan, C. P., and Scheribel, C. P.: The Effect Upon the Electrocardiograms of Patients With Regular Sinus Mechanism of Quinidin Sulphate. Am. J. M. Sc. **187**: 23, 1934.

Quinidine sulphate was administered to 19 patients with no general toxic effects. The electrocardiograms in the majority of these patients showed changes only

in regard to the T-wave within from twenty-four to seventy-two hours if orally administered and immediately if given intravenously. These changes varied from mild flattening to sharp inversion of the T-waves. The duration of the effect varied from three to six days on oral administration and three hours on intravenous administration. Changes in the QRS and P-R intervals are presumably effects produced by intoxicating doses.

Gold, Harry, and Klumpp, Margaret M.: On the Alleged Antagonism Between Digitalis and Diphtheria Toxin. Am. J. M. Sc. **185**: 509, 1933.

Results of this study show that digitalis does not afford any protection against poisoning by diphtheria toxin in the cat. It is probable that the same is true in man. It was also observed that very large doses of digitalis may hasten the death of animals poisoned by diphtheria toxin. Reference also is made to the fact that the routine use of digitalis in pneumonia does not lessen the mortality from that disease.

Evans, William, and Hoyle, Clifford: The Prevention and Treatment of Individual Attacks of Angina Pectoris (Angina of Effort). Quart. J. Med. **3**: 105, 1934.

A series of 122 patients with angina pectoris was observed over a period of three years with special reference to the comparative value of vasodilator drugs for the immediate treatment and prevention of attacks. The comparative results show that glyceryl trinitrate in tablet form when absorbed from the mouth is by far the most effective agent for relieving attacks and for their immediate prevention. Eighty-six per cent of the patients obtained great relief and a further 11 per cent moderate relief. Other preparations of glyceryl trinitrate and other remedies tried did not give such good results. Glyceryl trinitrate tablets should deservedly hold the first place in routine treatment. This is more advisable because they rarely cause objectionable symptoms; they are easy to store and carry so that they are always available for immediate use, and they are cheap. The only practical disadvantage is that they deteriorate in strength, especially when exposed to air and heat, so that they should be used preferably within two months of manufacture. Amyl nitrite proved to be disappointing for the relief of attacks, and it can be recommended only for those rare cases where glyceryl nitrate fails to relieve. It has the further disadvantage of being useless for the prevention of attacks.

The use of glyceryl trinitrate tablets immediately before expected anginal attacks is a safe means of preventing pain and should be used far more widely in routine treatment than it is at present. In our series 84.5 per cent patients obtained great benefit and a further 12.5 per cent moderate benefit by using the drug in this way. This is a greater measure of improvement than was found from any of the remedies tried in this investigation of continuous treatment. Most patients preferred to take the drug at their own discretion, and this method of administration proved more effective than when it was taken at short fixed intervals, except for those patients who could not predict attacks with certainty. No harmful effects were met from such treatment; though patients used the drug freely for upwards of two to three years, and often this enabled them to take more physical exertion and lead a fuller life than had previously been possible.

Gilchrist, A. Rae: The Action of Atropine in Complete Heart Block. Quart. J. Med. **2**: 483, 1933.

The response of ten individuals suffering from complete heart-block has been tested by the intravenous administration of $\frac{1}{30}$ gr. of atropine sulphate. Re-

peated electrocardiograms taken at intervals before and after the injection demonstrated that in every case studied this drug produced an acceleration of the ventricular rate.

The prevailing view, constantly repeated in the literature, that atropine has little or no effect on the frequency of the ventricles is incorrect and requires modification in the light of the peculiar character of the acceleration. The dose of atropine was sufficient to produce almost complete paralysis of the vagus. The maximum increase in ventricular rate was 47 beats per minute, representing a gain of almost 96 per cent over the initial rate. The minimum acceleration was 1.2 beats per minute, giving a percentage increase of 5.4. In only one case was the gain after atropine within the maximum range recorded under similar resting conditions.

The initial ventricular rate is the important factor in determining the amount of acceleration for a given dose of atropine, the higher the resting rate the greater the response to atropine. At low initial rates atropine produces but little acceleration. The coefficient of correlation between the rate before atropine and the amount of ventricular acceleration produced by it is +0.97—a very significant relationship.

The law expressing the degree of acceleration for a given initial ventricular rate has been represented by a straight-line formula. Actually, this is probably not the best expression. It would appear from the available data that a logarithmic curve might be the best expression, but the facts are too scanty to allow of its exact determination.

The use of atropine as a means of distinguishing the bradycardia of complete heart-block from other causes is therefore unreliable. Further work requires to be done on this subject with the object of determining the precise nature of the response to atropine in those cases of slow heart action in which complete heart-block is not present.

To obtain a decided effect on the ventricular rate, it is necessary to use an amount of atropine approaching the full paralyzing dose; $\frac{1}{30}$ gr. of atropine given intravenously in 1 c.c. of normal saline was found to be sufficient.

In contrast to the ventricular response, the auricular acceleration does not appear to bear any relation to the initial auricular rate. Further, the auricular range after atropine does not bear any relation to the ventricular. The amount of auricular acceleration varies irregularly from individual to individual. The auricular response probably reflects no more than the degree of vagal tone existing at the moment of injection.

The nature of the ventricular response suggests that the amount of acceleration is determined by the inherent rhythmicity of the specialized tissue at the center of impulse production. It is suggested that when the lesion producing the block is situated in the uppermost part of the conducting tract, a greater response will occur after atropinization than when the center of impulse production lies at a lower level in the specialized tissues.

As a converse of this, it may be suggested that vagal stimulation is more likely to be effective in slowing the idioventricular rate when the center of impulse production lies high in the conducting tract.

Gilchrist, A. Rae: The Action of Adrenalin in Complete Heart Block. Quart. J. Med. **2:** 499, 1933.

Twelve cases of complete heart-block have been tested with repeated subcutaneous doses of adrenalin in an attempt to discover the factors which govern the response of the heart to this drug.

After a subcutaneous dose the drug comes into action with surprising rapidity. Acceleration of auricles and ventricles may occur within from two to four minutes of the injection.

The amount of ventricular acceleration induced bears a striking relationship to the rate existing immediately before the injection. High initial rates are followed by little or no gain in rate, slow rates by pronounced acceleration. This means that the state of the heart at the time of the drug's administration determined the heart's response.

By plotting the observed increment against the corresponding initial rate, it is found that for a group of eight cases the reaction approximates to an almost perfect series of decreasing exponentials for increasing ventricular rates.

Within a certain range of dosage, the amount of adrenalin injected makes little or no difference to the ventricular response at a given ventricular rate. The optimum response to 0.5 c.c. adrenalin for various initial rates has been calculated and compared with the reaction observed after doses of 0.25, 0.75 and 1.0 c.c. in the same subjects. The gain in rate after these doses is to all intents similar to that recorded after 0.5 c.c. This implies that the response of the heart is determined, not by the size of a dose in the usual therapeutic range but by the rate of the heart existing at the time of the injection. In other words, for a given initial rate 0.25 c.c. of adrenalin will produce as much acceleration as a dose four times that amount.

This phenomenon is discussed in the light of the known laws which govern enzyme action. The independence of the size of the dose and the response recorded, suggests that a surface action is involved and that adrenalin is being absorbed on some (? enzyme) surface, as an essential condition of its action.

The observation that the initial rate determines the degree of acceleration finds support in blood pressure studies. Lyon has suggested that the reaction to adrenalin obeys Weber's law, in that the amount of elevation in the systolic blood pressure after uniform doses of adrenalin depended upon its level at the moment of the injection.

It has not been found possible to demonstrate as close a correlation between the initial auricular rate and its increment after adrenalin as that observed in the case of the ventricles. The auricular response is modified to some extent, particularly in those cases in which the magnitude of the ventricular response is maximum, that is, when the initial ventricular rate is relatively low.

It would appear probable that reflex vagal influences, induced by a marked ventricular reaction, limit the auricular response. The amount of limitation is apparently determined largely by the initial ventricular rate.

The course of the reaction to a subcutaneous dose of adrenalin varies as much in complete block as it does in the normal beating heart. The maximum auricular and ventricular reactions are not necessarily synchronous. As a general rule the auricles attain to the height of their reaction before the ventricles have completed their acceleration. An increased frequency of both chambers of the heart persists after the blood pressure rise has returned to its preexisting level. No untoward symptoms resulted from the use of the drug. Release from the block was not observed in any of the experiments performed upon these eight patients.

Reactions differing from those just described were encountered in four patients. One of these cases was a man who suffered from intermittent complete block. Tested with adrenalin during complete block, no change in the rhythm occurred, but a branch defect changed from one side of the heart to the other.

rested during two-to-one rhythm, complete block was induced. The direction of the main ventricular deflection varied according to the presence or absence of conduction through the main stem of the bundle. During half rhythm the ventricular complex in Lead III was directed downward, whereas during complete dissociation its direction was upward. The fact that this man's heart was unduly suspectible to adrenalin suggests that in cases of intermittent complete heart-block, the temporary failure of conduction, leading to transient complete dissociation, may perhaps be associated with the formation within the body of some subtle and complex chemical substance analogous to adrenalin or adenosine.

Hitchcock, Charles H., Camero, Anthony R., and Swift, Homer F.: Perivascular Reactions in Lung and Liver Following Intravenous Injection of Streptococci Into Previously Sensitized Animals. J. Exper. Med. **59**: 283, 1934.

Intravenous inoculation of small doses of nonhemolytic streptococci into previously sensitized rabbits is usually followed by the appearance of perivascular cellular aggregates in lung and liver. The characteristic cell in these aggregates is moderately large with vesicular nucleus, prominent nucleoli, clumped chromatin and basophilic cytoplasm. These characteristics together with the additional evidence of phagocytosis all indicate that the cell probably has its source in the reticuloendothelial system. Further study with vital staining methods and observations of its behavior toward parenterally introduced India ink should furnish more conclusive evidence as to its identity. Whether it is produced directly by the presence of the bacteria or secondarily to the destruction of some other cells or tissue is also a problem for the future to unfold. In addition, the lesions contain small lymphocytes and granulocytes.

This lesion is easily differentiated by architecture and cell content from normally occurring lymphoid aggregates and from spontaneous rabbit hepatic cirrhosis. This mononuclear response does not occur when the intravenous dose is large enough to cause death of the animal within twenty-four hours.

In spleen and lymph nodes the characteristic basophilic cells which normally occur in these organs are present in increased numbers.

Following intravenous treatment alone, or sensitization without intravenous treatment, the lesions occur much less frequently and when present are smaller and more sparsely found.

Inasmuch as in the present series of experiments this lesion was not found in normal animals and infrequently in those treated by the intravenous route alone, it is suggested that the preliminary sensitization serves to enhance the animal's reactivity to the antigen. In this way a small dose of bacteria is capable of eliciting the cellular phenomenon which in unsensitized animals appears only when larger doses of antigen are administered over longer periods of time. Too large a dose of antigen, however, results in shock and cell death rather than in proliferation.

Dawson, M. H.: A Comparative Study of Subcutaneous Nodules in Rheumatic Fever and Rheumatoid Arthritis. J. Exper. Med. **57**: 845, 1933.

The present communication presents a detailed study of the subcutaneous nodules in rheumatic fever and rheumatoid arthritis. It is believed that the study has shown that these lesions are highly characteristic of the two diseases and they represent different phases of the same fundamental, pathological process. It is probable that the two diseases represent different responses of affected individuals to the same etiological agent.

Keefer, Chester S.; Parker, Frederic, Jr.; Myers, Walter K.; and Irwin, Ralph L.: Relationship Between Anatomic Changes in Knee Joint With Advancing Age and Degenerative Arthritis. Arch. Int. Med. **53**: 325, 1934.

In a study of 100 knee joints from 77 consecutive patients who died of various diseases the following facts were determined:

Anatomical changes were noted with increasing frequency with advancing age.

The patella showed alterations in 81 per cent of the cases, the interpatellar groove in 65 per cent, the lateral condyle of the tibia in 64 per cent, the medial condyle of the tibia in 55 per cent, the medial condyle of the femur in 43 per cent, and the lateral condyle in 36 per cent.

The erosions were commonest over the areas of contact which were subjected to the greatest movement, strain, weight-bearing, and injury.

The changes were identical in males and females, and there was no relationship between the extent of the lesions in the joints and the symptoms referable to the joints.

There was no correlation between the lesions in the joints and the degree of arteriosclerosis or any other particular type of disease process.

The gross anatomical changes were indistinguishable from those previously described in degenerative arthritis.

The various factors which are of importance in the development of degenerative arthritis are discussed. They include the aging of tissue, wear and tear, strain, trauma, occupation, and static deformities.

From these observations it seems difficult to escape the conclusion that the changes seen in the joints with increasing frequency with advancing age are identical with those which have been described previously as characteristic of degenerative arthritis. If this is true, there is justification for the belief that degenerative arthritis is a process associated with the aging of the tissues of the joints. This conception is essential for a complete understanding of the pathogenesis of this disorder. Added to the process of involution, such factors as gross trauma, hemorrhage and static deformities exaggerate the condition. The end-result depends upon the summation of these factors.

Weinstein, Israel, and Styron, Norma C.: Bacteriologic Study of Throats in Rheumatic and Nonrheumatic Fever With Special Reference to Hemolytic Streptococci. Arch. Int. Med. **53**: 453, 1934.

The present investigation includes 321 cases and 840 cultures from Montefiore and Bellevue Hospitals, New York City. Forty-six per cent of the subjects were patients with rheumatic fever. Fifty-eight per cent of the cultures were taken from this group. The remainder were taken from normal persons and from patients suffering from diseases other than rheumatic fever; these constituted the control group. In more than one-third of the cases of rheumatic fever and in more than one-half of the cultures taken from this group the patients were under fifteen years of age.

The percentage of cultures which were positive for the hemolytic streptococcus taken from the throats of patients with rheumatic fever was approximately the same as that found in other persons. In these positive cultures, the hemolytic streptococcus appeared to be no more abundant in those obtained from patients with rheumatic fever than in those from other persons.

Throat cultures of patients with rheumatic fever taken during an infection of the upper respiratory tract showed no greater incidence of hemolytic streptococci than those from other persons who were suffering from a cold or from sore throat.

Infections of the upper respiratory tract were found associated with *Streptococcus hemolyticus* more frequently in young persons who were suffering from rheumatic fever than in older patients with this disease.

Hemolytic streptococci were found more frequently associated with infection of the upper respiratory tract in rheumatic persons who had not had their tonsils removed than in those on whom tonsillectomy had been performed.

Green-producing streptococci were present in all the cases and in 99 per cent of the cultures. They predominated in 69 per cent of the cases and in 73 per cent of the cultures.

Indifferent streptococci were present in 96 per cent of the cases and in 88 per cent of the cultures. They predominated in 3 per cent of the cultures.

In the groups studied, exacerbations of acute rheumatic fever occurred as frequently when there was no infection of the throat as when there was.

The fact that the majority of those in whom exacerbations of rheumatic fever occurred were persons who had hemolytic streptococci in their throats suggests a possible relationship between this organism and the reappearance of the symptoms.

Schlesinger, Bernard, and Signy, A. Gordon: Precipitin Reactions in the Blood of Rheumatic Patients Following Acute Throat Infections. Quart. J. Med. 2: 255, 1933.

Streptococcal precipitins can be demonstrated in the blood of rheumatic patients following acute streptococcal throat infections. Their formation is delayed until from the second to fourth week from the onset of nasopharyngeal infection (the end of the silent period), and their appearance in most cases foreshadows a tendency to a relapse of acute rheumatism.

The precipitin corresponds to the type of streptococcus responsible for the throat infection, but a certain amount of cross precipitin formation may occur. The formation of precipitin is regarded as one of the manifold reactions which take place in the patient's defense mechanism during the silent period. There is thus time for prophylactic measures if the throat infection has not passed unnoticed. Concentrated aspirin therapy during this period undoubtedly prevents serious relapses in many cases. It is not infallible and further research work is urgently required to discover some other method which is still more reliable.

Laws, Clarence L., and Levine, Samuel A.: Clinical Notes on Rheumatic Heart Disease With Special Reference to the Cause of Death. Am. J. M. Sc. 186: 833, 1933.

One hundred and forty-eight cases of rheumatic heart disease were studied to ascertain the cause of death. It was found that congestive heart failure accounted for only 33.1 per cent of the fatalities, acute rheumatic carditis for 23 per cent, peripheral emboli and thromboses for 11.5 per cent, subacute bacterial endocarditis for 29 per cent, and 3.4 per cent of the patients died of miscellaneous cardiovascular accidents like angina pectoris or acute pulmonary edema.

The groups of congestive failure and emboli and thromboses were the oldest, subacute bacterial endocarditis a little younger, and acute rheumatic carditis the youngest.

Those that had aortic valvular disease alone were the oldest (52.5 years). The mitral cases came next (42.8 years) and the cases with combination of aortic, mitral and tricuspid were youngest (30 to 35 years).

There were more than twice as many females as males dying of acute rheumatic carditis, the relation was reversed in the group dying of emboli and

thromboses, and the proportion was three to two on the side of males in the subacute bacterial endocarditis group.

A past history of rheumatic fever or chorea was not found with equal frequency among the various groups. Athough the authors believe that stenosis of any of the valves is, except in rare instances of congenital heart disease, practically invariably due to rheumatic infection, the multiform character of the early illness prohibits obtaining a positive history in many instances. The greater the number of valves involved, the more frequently was a positive past history obtained. This is true for two reasons: such patients are more liable to have had more than one infection and they die at a younger age, so that the early illnesses are not forgotten. This explains why patients with aortic stenosis who die at an old age less frequently have a positive past history.

In speaking of valvular lesions in this review, except for those cases dying of subacute bacterial endocarditis, stenosis to a greater or lesser extent is meant. A striking finding was the great frequency of involvement of the aortic and tricuspid valves. When the tricuspid valve was involved, the mitral was always diseased as well, and frequently the aortic.

Auricular fibrillation was almost invariable in the emboli and thrombi group, very common in those dying of congestive heart failure, much less common in the acute rheumatic carditis group and practically absent in those who died of subacute bacterial endocarditis. The presence of mitral stenosis is the most common accompaniment of auricular fibrillation; although this irregularity occurs occasionally in patients who have only aortic stenosis.

The average weight of the heart of those dying with congestive failure was 617 gm., of acute rheumatic carditis or emboli and thromboses about 550 gm., and of subacute bacterial endocarditis 449 gm. The average weight of the heart in cases of aortic stenosis was 669 gm., of mitral stenosis 474 gm., and of both 663 gm. When the tricuspid was involved in combination with other valves, the average weight was about 550 gm. The presence of adhesive pericarditis increased the average weight by about 120 gm. The average weight of 43 cases with adhesive pericarditis was 654 gm., and of 62 cases with a normal pericardium was 534 gm.

Pericarditis with or without adhesions was less frequent in the older patients. It was most common in the group with acute rheumatic carditis, fairly frequent in those with congestive heart failure, and very rare with subacute bacterial endocarditis.

Book Reviews

DISSECTING ANEURYSMS. By T. Shennan. (A report issued by the Medical Research Council.) London. Published by His Majesty's Stationery Office, 1934, 136 pages.

This very complete study of dissecting aneurysms by Professor Shennan of Aberdeen is based upon an analysis of 300 reported cases, including seventeen investigated by the writer himself.

Both the pathological and the clinical features of the condition are discussed fully and interestingly. The author finds that degeneration of the media is a factor common to all cases and that in a majority of instances the media gives way before the intima. Much the commonest cause of death is rupture into the pericardial sac. It is interesting that syphilis seems to play a relatively unimportant etiological rôle in this form of aneurysm.

The monograph includes a historical review of the subject and a full bibliography. It is procurable in this country from the British Library of Information, 270 Madison Avenue, New York City.

L. A. C.

LE DUALISME DE LA CONTRACTION CARDIAQUE. By F. Henrijean. Paris, Masson et Companie, 1933, pp. 350.

In this account of the mechanism of heart action, which comprises a full 350 pages, the author gives interpretative analyses, theoretical deductions, numerous tracings of electro- and mechanograms, and a fairly thorough review of a considerable amount of the experimental work in the field.

"The dual mechanism of the cardiac contraction," as announced by the title of the monograph, arouses an expectant interest, but one searches vainly for a concise statement of the real significance of this phrase. The first section of the book is devoted to the electrocardiogram and its relation to certain variations in the contractile response of the heart. In this portion consideration is given to the response of the embryonic heart of the chick, to the action of chloroform, and to the electrical response of the apparently quiescent heart. In each instance the form of the electrical disturbance is discussed in the light of one type of curve which is indicative of the physiological excitatory function of the heart and another which denotes the predominantly energy-transforming phase of cardiac response. Two remaining divisions of the book have to do with interpretations of the form of the electrocardiogram in their bearing on the postulated dual mechanism, and with the rôle played by the vagus and sympathetic nerves in this twofold type of response.

From the standpoint of the essentially new observations in the book it may be questioned whether sufficient warrant is given for all the space devoted to the subject; in fact, much philosophical material might be eliminated without detracting from the main thesis.

D. J. E.